10/523,111 Page 3

chain bonds :

2-12 7-13 10-14 18-20 19-21

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12 14-15 14-19

15-16 16-17 17-18 18-19

exact/norm bonds :

1-2 1-6 2-3 2-12 3-4 4-5 5-6 7-8 7-12 7-13 8-9 9-10 10-11 11-12

exact bonds :

10-14 18-20 19-21

normalized bonds :

14-15 14-19 15-16 16-17 17-18 18-19

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom 12:Atom 13:CLASS 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom 20:CLASS 21:CLASS

L1 STRUCTURE UPLOADED

0

=> d 11

L1 HAS NO ANSWERS

L1 STR

rings not isolated

Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 10:11:25 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 128 TO ITERATE

100.0% PROCESSED

128 ITERATIONS

12 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 1882 TO 3238

PROJECTED ANSWERS: 33 TO 447

L2 12 SEA SSS SAM L1

Habte 02/09/2007

10/523,111 Page 4

=> s l1 sss full FULL SEARCH INITIATED 10:11:31 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 2760 TO ITERATE

100.0% PROCESSED 2760 ITERATIONS 241 ANSWERS

SEARCH TIME: 00.00.01

L3 241 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION 172.10 172.31

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L4 22 L3

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L4 ANSMER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
DOCUMENT NUMBER:
143:229869 Preparation of phthalazinone derivatives as PDE4 inhibitors
INVENTOR(S): Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Christians, Johannes A. M.; Menge, Wiro M. P. B.; Sterk, Geert Jan
PATENT ASSIGNEE(S): SOURCE: PIXXD2
DOCUMENT TYPE: CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: English

PATENT NO. KIND DATE APPLICATION NO. DATE WO 2005075457 WO 2005075457 20050818 WO 2005-EP50417 20050201 A1 A8 20060302 AB 20060302

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BM, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, RR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, ND, MG, MK, NN, MM, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZM, SM

RW: BN, GH, GM, KE, LS, MN, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, PI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BP, BJ, CP, CG, CI, CM, GA, GN, GG, GM, ML, MR, NE, SN, TD, TG

EP 1720854

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LI, LU, MC, NL, PL, FT, RO, SE, SI, SK, TR
PRIORITY APPLN. INFO:

EP 2004-2423

A 20040204

WO 2005-EP50417

W 20050201

MARPAT 143:229869

OTHER SOURCE(S):

STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I [R1 and R2 are both H or together from an addnl. bond; R3 = (un)substituted phenyl; R4 = OH, alkoxy, NHR5, etc.; R5 = OH, alkoxy or alkoxyalkyl; n = 0, 2, 3, or 4) and their pharmaceutically acceptable salts, are prepared and disclosed as PDRs inhibitors. Thus, e.g., II was prepared by coupling of (48S,88R)-4-(3,4-dimethoxy-phenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (preparation given) with

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

862462-50-8 CAPLUS
Piperazine, 1-[4-[4-[468,8aR]-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-1,4-dioxobutyl]-4-methyl-, (2E)-2-butenedioate (9CI) (CA INDEX NAME)

Absolute stereochemistry.

CRN 110-17-8

Habte

ANSMER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) different methods utilizing cAMP and it was revealed that compds of the invention displayed -logICSO values in the range of 8.4 up to 10.4 mol/L. I as inhibitor of PDE4 should prove useful in the treatment of airway disorders. Pharmaceutical compns. comprising I are disclosed. 85246247-3P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of phthalazinone derive. as PDE4 inhibitors) 822462-47-3 CAPLUS
1-Piperidinebutanoic acid. (485,888,4-13,4-dimethoxyphenyl)-48,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-y-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

862462-48-4P 862462-50-8P 862462-51-9P
862462-53-1P 862462-54-2P 862462-55-3P
862462-56-4P 862462-55-5P 862462-56-6P
862462-59-7P 862462-60-0P 862462-61-1P
862462-62-P 862462-63-3P
862462-62-P 862462-63-3P
862462-62-P 862462-63-3P
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phthalaxinone derivs. as PDE4 inhibitors)
862462-48-4 CAPLUS
Morpholine, 4-[4-[4-[(485,88R)-4-(3,4-dimethoxyphenyl)-48,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalaxinyl]-1-piperidinyl]-1,4-dioxobutyl]-

Absolute stereochemistry.

ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN CMP C4 H4 O4

но₂с В со₂н

862462-51-9 CAPLUS
1-Piperidinebutanamide, 4-{(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-y-oxo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

862462-53-1 CAPLUS
Piperazine, 1-[4-[4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-1,4-dioxobutyl]-4-[2-(2-oxo-1-pyrrolidinyl)ethyl]-, (2E)-2-butenedioate (9CI) (CA INDEX NAME)

CRN 862462-52-0 CMF C35 H48 N6 Q6

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CRN 110-17-8 CMF C4 H4 O4

Double bond geometry as shown.

% 62462-54-2 CAPLUS 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- $\alpha$ -oxo-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.

862462-57-5 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalezinyl)-N,N-dimethyl-a-oxo-(9CI) (CA INDEX NNB)

Absolute stereochemistry.

862462-58-6 CAPLUS 1-Piperidineacetamide, 4-{{4aS,5aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-hydroxy- $\alpha$ -oxo-{9CI} (CA INDEX INDEX INDEX

Absolute stereochemistry.

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.

RN 862462-56-4 CAPLUS
CN Piperazine,
1-[[4-[(48,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]oxoacetyl]-4-methyl-,
monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 862462-59-7 CAPLUS
CN 1-Piperidineacetamide,
4-{{4as,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,6,7,8,8a-hexahydro-1-oxo-2{1H}-phthalazinyl}-a-oxo-{9CI} (CA INDEX NAME)

Absolute stereochemistry.

862462-60-0 CAPLUS Morpholine, 4-[{4-[(4s,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]oxoacetyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 862462-61-1 CAPLUS
CN Piperazine, 1-[[4-[[4-5],8-aR]-4-{3,4-dimethoxyphenyl}]-4-a,5,6,7,8,8-a-hexahydro-1-oxo-2(IH)-phthalazinyl]-1-piperidinyl]oxoacetyl]-4-methyl-(SCI) (CA INDEX NAME)

Absolute stereochemistry.

RN 862462-62-2 CAPLUS
CN 1-Piperidineacetic acid, 4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-a-oxo-, 2,2-dimethylhydrazide (9CI) (CA INDEX NAME)

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4as,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HC1

RN 785047-47-4 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2-(4piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 862462-64-4 CAPLUS
CN 1-Piperidineacetic acid, 4-[{4aS,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalasinyl]-α-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ADBOIUTE 6

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) Absolute stereochemistry.

RN 862462-63-3 CAPLUS
CN 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8at-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(2-methoxyethyl)-a-oxo-(9CI)
(CA INDEX NAME)

Absolute stereochemistry.

T 380226-97-1P 785047-47-4P 862462-64-4P 862462-65-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent). (preparation of phthalazinone derive. as PDE4 inhibitors) N 380226-97-1 CAPLUS

L4 ANSWER 1 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 862462-65-5 CAPLUS
CN 1-Piperidineacetic acid, 4-{(4aS,8aR)-4-{3,4-dimethoxyphenyl}-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]-α-oxo-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

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L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2005:823688 CAPLUS CAPLUS 143:229868 Prency 68

Preparation of piperidinyl pyridazinone derivatives

PDE4 inhibitors PDE4 inhibitors
Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard;
Kley, Hans-Peter; Christiaans, Johannes A. M.; Menge,
Wiro M. P. B.; Sterk, Geert Jan
Altana Pharma A.-G., Gernany
PCT Int. Appl., 53 pp.
CODEN: PIXXD2
Patent
English
1 INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT:

PATE	NT INF	PORMATI	ON:															
	PATEN	T NO.			KIN	KIND DATE A						ION	DATE					
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	WO 20	050754	56		Al		2005	0818		WO 2	005-	EP50	415		2	0050	201	
	WO 20	050754	A8		2006	0302												
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		CN.	co,	CR,	CU,	cz,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,	
		GE.	GH,	GM,	HR,	HU,	ID.	IL,	IN,	IS.	JP,	KE,	KG,	KP,	KR,	KZ.	LC,	
		LK.	LR.	LS,	LT.	LU.	LV.	MA,	MD,	MG,	MK,	MN,	MW,	MX.	MZ,	NA.	NI,	
		NO.	NZ.	OM,	PG.	PH,	PL,	PT.	RO.	RU.	SC.	SD,	SE,	SG,	SK,	SL.	SY.	
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SM																		
	F	W: BW.	GH,	GM.	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	
		AZ.	BY,	KG.	KZ.	MD.	RU,	TJ,	TM.	AT.	BE,	BG.	CH,	CY.	CZ.	DE.	DK,	
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WO 2005-EP50415 W 20050201

OTHER SOURCE(S):

MARPAT 143:229868

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Title compds. I [R1 and R2 independently = alkyl; R3 = (un)substituted phenyl; R4 = CORS, S(0)2R6(CH2)nCOR7 or CO(CH2)mR8; R5 = alkyl, NR9R10 or (un)substituted phenyl; R6 = alkyl, NR1R12 or (un)substituted phenyl; R7 = NR13R14; R8 = NR1SR16; R9-16 independently = H, alkyl, cycloalkyl,

etc.;  $n = 1 \text{--}4; \; m = 1 \text{--}4\}$  and their pharmaceutically acceptable salts, are prepared

ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

# ●x HCl

RN 862578-20-9 CAPLUS
CN 1-Piperidineacetamide,
4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl]-(9C1) (CA INDEX NAME)

Habte

862578-21-0 CAPLUS
Piperidine, 4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-((2,5-dioxo-1-pyrrolidinyl)acetyll- (9C1) (CA INDEX

RN 862578-22-1 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-

ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) and disclosed as PDE4 inhibitors. Thus, e.g., II was prepd. by coupling of 6-(3,4-dimethoxypheny)1-4,4-dimethyl-2-piperidin-4-yl-4,5-dihydro-2H-pyridazin-3-one (prepn. given) with 2-cyanobenzenesulfonyl chloride. The inhibitory activity of I was evaluated using scintillation proximity

inhibitory activity of I was evaluated using scintillation proximity assay
and it was revealed that selected compds. of the invention displayed -logiCSO values in the range of 7.60 up to 9.68 mol/L. I as inhibitor of PDE4 should prove useful in the treatment of airway disorders.
Pharmaceutical compns. comprising I are disclosed.

IT 862578-18-5P 862578-19-6P 862578-20-9P 862578-21-0P 862578-21-P 862578-21-P 862578-22-P 862578-22-P 862578-23-P 862578-23-P 862578-23-P 862578-23-P 862578-23-P 862578-23-P 862578-30-P 862578-30-P 862578-31-2P 862578-31-2P 862578-31-2P 862578-31-P 862578-37-8P 862578-39-P 862578-39-OP RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of piperidinyl pyridazinone derivs. as PDE4 inhibitors) 863578-18-5 CAPLUS
Piperidine, 1-(12-cyanophenyl)sulfonyl)-4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl)- (9CI) (CA INDEX NAME)

862578-19-6 CAPLUS
Morpholine, 4-[3-{4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-piperidinyl}-1-oxopropyl]-, hydrochloride (9CI) (CA INDEX NAME)

ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) 1(4H)-pyridazinyl]-1-[(2-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

862578-24-3 CAPLUS
Piperidine, 1-[(4-cyanophenyl)sulfonyl]-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)

862578-25-4 CAPLUS
Piperidine, 4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-l(4H)-pyridazinyl}-1-[(2-(trifluoromethoxy)phenyl]sulfonyl)- (9Cl) (CA INDEX NAME)

862578-26-5 CAPLUS
Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-(2-methoxybenzoyl)- (9Cl) (CA INDEX NAME)

02/09/2007

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 862578-27-6 CAPLUS
CN Piperidine, 1-[(3-cyanophenyl)sulfonyl]-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)

RN 862578-28-7 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 862578-29-8 CAPLUS
CN Piperidine, 4-[3-4], 4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo[1(H)-pyridasinyl)-1-[(3-methylphenyl)sulfonyl]- (9CI) (CA INDEX RAME)

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Cont

RN 662578-30-1 CAPLUS
CN 1-Piperidinesulfonamide, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridszinyll-N,N-dimethyl- (SCI) (CA INDEX NAME)

RN 862578-31-2 CAPLUS
CN 1-Piperidineacetamide, 4-[3-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 862578-32-3 CAPLUS
CN Piperidine,
1-benzoyl·4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)

RN 862578-33-4 CAPLUS
CN 1-Piperidineacetamide,
4-[3-(3,4-dimethoxyphenyl)-5,5-diethyl-5,6-dihydro6-0xo-1(4H)-pyridazinyl)-, hydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

•x HC

RN 862578-34-5 CAPLUS
CN Piperidine, 1-[(2-cyanophenyl)sulfonyl)-4-[3-(3,4-dimethoxyphenyl)-5,5-diethyl-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)- (9CI) (CA INDEX NAME)

RN 862578-35-6 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-[(3,5-dioxo-4-morpholinyl)acetyl]- (9CI) (CA INDEX NAME)

RN 862578-36-7 CAPLUS CN Piperidine, 02/09/2007 dimethoxyphenyl)-5,5-diethyl-5,6-dihydro-6-oxo-1(4H)-

## 10/523,111

### Page 10

ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) pyridazinyl]-1-(2-methoxybenzoyl)- (9CI) (CA INDEX NAME)

862578-37-8 CAPLUS
Piperidine, 4-[3-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-5,6-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-[(4-methyl-1-piperazinyl)acetyl)- (9CI) (CA INDEX NAME)

862578-38-9 CAPLUS
Piperidine, 4-[3-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-1-{(2,5-dioxo-1-pyrrolidinyl)acetyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

862578-48-1 CAPLUS
3(2H)-Pyridazinone,
(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4,5-dihydro-4,4-dimethyl-2-(4-piperidinyl)-, hydrochloride (9CI) (CA
INDEX NAME)

●x HCl

862578-54-9 CAPLUS
3(2H)-Pyridezinone, 6-(3,4-dimethoxyphenyl)-4,4-diethyl-4,5-dihydro-2-(4-piperidinyl)-, hydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

862578-39-0 CAPLUS
Piperidine, 1-{(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl}-4-{3-(3,4-dimethoxyphenyl)-5,6-dihydro-5,5-dimethyl-6-oxo-1(4H)-pyridazinyl]-(9CI)
(CA INDEX NAME)

IT 862578-44-7P 862578-48-1P 862578-54-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinyl pyridazinone derivs. as PDE4 inhibitors)
RN 862578-44-7 CAPLUS
CN 3 (2H)-Pyridazinone,
6-(3,4-dimethoxyphenyl)-4,5-dihydro-4,4-dimethyl-2-(4-piperidinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

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THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

02/09/2007

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2005:232615 CAPLUS COPYRIGHT 2007 ACS ON STN 142:291403 Use of Phonon Copyright 2007 ACS ON STN 2005:232615 CAPLUS Use of Phonon Copyright 2007 ACS ON STN 2005:232615 CAPLUS Use of Phonon Copyright 2007 ACS ON STN 2005:232615 CAPLUS Use of Phonon Copyright 2007 ACS ON STN 2005:232615 CAPLUS Use of Phonon Copyright 2007 ACS ON STN 2005:232615 CAPLUS USE OF Phonon Copyright 2005:2326

142:291403
Use of phosphodiesterase 4 (PDR4) inhibitors for the treatment of diabetes mellitus
Hauser, Daniels; Kanauer, Guido; Grundler, Gerhard;
Schmidt, Beate; Kemkowski, Joerg; Kley, Hans-Peter Altana Pharma A.-G., Germany
PCT Int. Appl., 50 pp.
CODEN: PIXXD2

INVENTOR (S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: Patent English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

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	WO	2005	0232	53		A1		2005	0317	1	WO :	2004-1	3P52	005		2	0040	902
	WO	2005	0232	53		A8		2006	0302									
		W:	AE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	, BG,	BR,	BW,	BY,	BZ,	CA,	CH,
			CN.	co.	CR.	CU.	CZ,	DE,	DK,	DM,	DZ	, EC,	EE,	EG.	ES,	PI,	GB,	GD,
			GE.	GH.	GM,	HR.	HU.	ID,	IL,	IN.	IS.	JP,	KE,	KG,	KP,	KR,	KZ,	LC.
			LK.	LR.	LS.	LT.	LU.	LV.	MA.	MD,	MG	, MK,	MN,	MW,	MX,	MZ,	NA.	NI,
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WO 2004-EP52005

W 20040902

RN 449760-14-9 CAPLUS CN Piperidine, 4-{{4aS,8aR}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry.

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-[(4a5,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl)-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) 2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-15-0 CAPLUS CN Piperidine, 4-{{4a5,8aR}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-{(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-20-7 CAPLUS 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-21-8 CAPLUS
1-Piperidinecarboxamide, 4-[{4aS,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- {9CI} (CA

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-22-9 CAPLUS 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl|-N-(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

449760-23-0 CAPLUS
Piperidine, 4-[(485,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-26-3 CAPLUS
CN Morpholine,
4-[[4-[(4aS,8sR)-4-[3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(lH)-phthalazinyl)-1-piperidinyl]carbonyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

PAGE 1-A

PAGE 2-A

RN 449760-24-1 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4eS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3, 4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued) PAGE 2-A

449760-29-6 CAPLUS 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4e,5,8,8a-tetrahydro-2-(1-thieno[2,3-d)pyrimidin-4-yl-4-piperidinyl)-, (4eS,8eR)- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2-

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN NAME) (Continued)

Absolute stereochemistry.

449760-42-3 CAPLUS
2,3-Piperazinedione, 1-{[4-{(4aS,8aR)-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1h)-phthalazinyl]-1-piperidinyl}carbonyl]-4-ethyl-(SCI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-47-8 CAPLUS
CN Piperidine,
4-[(4a5,8aP.4-(1,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) pyrimidinyl)-4-piperidinyl]-, (4as,8ar)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-35-4 CAPLUS
CN Morpholine,
{-[{4-[{44.5,8aR}}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[(4as,SaR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N-(1-methylethyl)- (9CI) (CA INDEX

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-48-9 CAPLUS 1(2H)-Phthalezinone, 2-{1-{2-(4-amino-3,5-dichloropheny1)-2-oxoethy1}-4-piperidiny1)-4-(3,4-dimethoxypheny1)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-49-0 CAPLUS
CN 1(2H)-Phthalexinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[{2-cxo-2H-1-benzopyran-7-y1)methyl}-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-50-3 CAPLUS

CN Morpholine,
4-[(4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl)-1-piperidinyl)acetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4e,5,8,8e-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-52-5 CAPLUS
1(2H)-Phthalazinone,
4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3pyridinylmethyl)-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)

Absolute stereochemistry.

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2-pyridinylmethyl}-4-piperidinyl]-, {4aS,8aR}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-56-9 CAPLUS 1(2H)-Phthalazinone, 3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-{1,2,3-thiadiazol-4-yl}phenyl}methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

449760-57-0 CAPLUS
Benzoic acid, 4-{[(4-[(4as,8aR)-4-{3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyllacetyl]amino}-, ethylester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-58-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

RN 596102-01-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(1-methylethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

596102-07-7 CAPLUS

Absolute stereochemistry.

RN 596102-09-9 CAPLUS
CN Piperidine,
4-[(4aS,8aR]-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl]-1-[[4-[2-(dimethylamino)ethyl]-1-piperazinyl]acetyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 3 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

REFERENCE COUNT:

THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2004:1036929 CAPLUS DOCUMENT NUMBER: 142:16825 Composition comprising a PDE4

INVENTOR (S):

142:16825 Composition comprising a PDE4 inhibitor and a PDE5 inhibitor Dunkern, Thoreten; Hatzelmann, Armin; Schudt, Christian; Grimminger, Friedrich; Ghofrani, Hossein Ardeschir Argeschir Altana Pharma A.-G., Germany PCT Int. Appl., 43 pp. CODEN: PIXXD2 Patent

PATENT ASSIGNEE(S): SOURCE: DOCUMENT TYPE: LANGUAGE:

English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2004103407 A3 2005122 WO 2004-EP50869 20040519

WO 2004103407 A3 20050217

W: AR. AG, ALI, AM, AT, AU, AZ, BA, BB, BG, BR, BM, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TT, TZ, UA, UG, US, UZ, VC, VN, YU, 2A, 2M, 2M, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GM, ML, MR, NE, SN, TD, TO

AU 2004247149 A1 20041202 AU 2004-241749 20040519

CA 2525946 A1 20041202 CA 2004-2525946 20040519

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, RD, 2004010126 A2 200405136

AB 2004010126 A2 2004010126 APPLICATION NO. PATENT NO. KIND DATE DATE 20060523 20060621 20061214 20060504 20051214 WO 2004-EP50869

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB The invention relates to the combined administration of a PDE4 inhibitor and a PDE5 inhibitor for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or phosphodiesterase 5 (PDE5) activity is detrimental. Patients were administered orally one tablet of Roflumilase and once daily a tablet of Viagra. An example of another selected PDE4 inhibitor is 1.

IT 449760-14-9 449760-15-0 449760-16-1
449760-17-2 449760-19-4 449760-20-7
449760-17-2 449760-21-9-4 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-21-0 449760-31-0 449760-31-0 449760-41-0 449760-41-0 449760-41-0 449760-41-0 449760-31-0 449760-41-0 449760-31-0 44

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-15-0 CAPLUS CN Piperidine, 4-[(445,887)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrshydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-20-7 CAPLUS
1-Piperidineczhoxamide, 4-[(4a5,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-21-8 CAPLUS
1-Piperidinecarboxamide, 4-[{4a5,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-{1,1-dimethylethyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-[(4a8,8aR]-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-[{4aS,8aR}-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-ox-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-22-9 CAPLUS 1-Piperidinecarboxamide, 4-{(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

449760-23-0 CAPLUS
Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl}-(SCI) (CA INDEX NAME)

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued)

PAGE 2-A

RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-27-4 CAPLUS
1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-,monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

olute stereochemistry.

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphemyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo(3,4-d)pyrimidin-4-yl)-4-piperidinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS CN 1(2H)-Phthalezinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-26-3 CAPLUS
CN Morpholine,
4-[[4-[(48,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

449760-29-6 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno(2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4a5,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)

PAGE 1-A

PAGE 2-A

RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) Oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (CA INDEX NAME)

Absolute stereochemistry.

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[{4aS,8aR}-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-terrahydro-1-oxo-2(1H)-phthalazinyl}-N-(1-methylethyl)- {9CI} (CA INDEX NAME)

Absolute stereochemistry.

449760-42-3 CAPLUS
2,3-Piperazinedione, 1-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl-(9CI) (CA INDEX RAME)

Absolute stereochemistry.

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-31-0 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl]methyl]-4-piperidinyl]-, monohydrochloride,
(4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HC1

RN 449760-35-4 CAPLUS CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-47-8 CAPLUS
Piperidine,
[(4as,6as]-4-(1,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

RN 449760-50-3 CAPLUS
CN Morpholine,
4-[[4-[(44S,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-0xo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)-

L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-51-4 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4e,5,8,8e-tetrahydro-2-(1-{2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-52-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4eS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-55-8 CAPLUS
CN 1-Piperazineethanamine,
4-[(48,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-0xo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-56-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[4(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

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L4 ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(2pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-54-7 CAPLUS
CN Morpholine,
4-[[4-[(48,8aR)+4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-{[[4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9CI) (CA INDEX NAME)

449760-58-1 CAPLUS
1-Piperidineacetamide, 4-[(4a5.8aR)-4-(3.4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

LA ANSWER 4 OF 22 CAPLUS COPYRIGHT 2007 ACS OR STN (Continued)

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-15-0 CAPLUS
Piperidine,
[(4aS,8aB,4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperiddine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
DOCUMENT NUMBER:
11TLE: 2004:996001 CAPLUS
11TLE: 141:406065
COmposition comprising a PDE-4 inhibitor and a THF-alpha antagonist
THF-alpha antagonist
Barriag, Johannes; Weimar, Christian
Altana Pharma AG, Germany
PCT Int. Appl., 29 pp.
CODEN: PIXXD2
Patent INFORMATION:
English
1
TATENT INFORMATION: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: MO 2004098633 A1 20041118 MO 2004-EP50748 20040510
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BM, BY, BZ, CA, CH,
CN, CO, CC, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KB, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NA, NI,
NO, NZ, OM, PO, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SY,
TJ, TM, TN, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RN-BM, GH, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BP, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
PRIORITY APPLN. INFO: PRIORITY APPLN. INFO.:

PR 2003-10581

AB The invention relates to the combined administration of a PDE4 inhibitor and a TNF0 antegonist selected from the group consisting of etanercept, onercept and pegsunercept for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or tumor necrosis factor alpha (TNF0) activity is detrimental.

If 449760-14-9 449760-15-0 449760-16-1 449760-14-9 449760-13-0 449760-16-1 449760-12-8 449760-19-4 49760-20-7 449760-21-8 449760-29-4 49760-20-7 449760-21-8 449760-29-9 449760-23-0 449760-24-1 449760-25-2 449760-30-9 449760-31-9 449760-31-6 449760-31-6 449760-31-6 449760-31-6 449760-31-6 449760-51-6 749760-51-6 74976

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Absolute stereochemistry.

449760-17-2 CAPLUS 449760-17-2 CAPLUS
1-Piperidinepentanoic acid,
4a5,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl}-8-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-{{4aS,8aR}-4-(3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-20-7 CAPLUS
CN 1-Piperidinecarboxamide, 4-{(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-21-8 CAPLUS
CN 1-Piperidinecarboxamide, 4-[{4aS,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrshydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

RN 449760-24-1 CAPLUS
CN 1(2H)-Phthalazinone.
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl}-, (4eS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-22-9 CAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 449760-23-0 CAPLUS

RN Piperidine, 4-[(468,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1
cox-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4e,5,8,8a-tetrahydro-2-[1-(4pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

RN 449760-26-3 CAPLUS
CN Morpholine,
4-[[4-[468, 58R]-4-[3,4-dimethoxyphenyl]-4e,5,8,8e-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)
Absolute stereochemistry.

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3, 4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{1methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

L4 ANSMER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued No. 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyrimidinyl)-4-piperidinyl]-, (4a3,8aR)- (9CI) (CA INDEX NAME) (Continued)

Absolute stereochemistry.

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[[4-[[48,8aR]-4-(3,4-diethoxyphenyl]-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl}-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalaxinyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

449760-29-6 CAPLUS 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

449760-30-9 CAPLUS

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

449760-42-3 CAPLUS
2,3-Piperazinedione, 1-[[4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-terrahydro-1-oxo-2(1H)-phthalazinyl}-1-piperidinyl}carbonyl}-4-ethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN: 449760-47-8 CAPLUS
CN Piperidine,
4-{(448,548)-4-{3,4-diethoxyphenyl}-44,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-(4-pyridinylcarbonyl)-(9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-48-9 CAPLUS
1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-49-0 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4e,5,8,8a-tetrahydro-2-[1-{{2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl}-, (4as,8aR)- (9CI) (CA

L4 ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

RN 449760-52-5 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(3-pyridinylmethyl)-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA INDEX NAME)

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN INDEX NAME) (Continued)

Absolute stereochemistry.

449760-50-3 CAPLUS

RN 449760-50-3 CAPLUS .

CN Morpholine.
4-[{4-[{48,5aR},-4-{3,4-dimethoxyphenyl})-4a,5,8,8a-tetrahydro1-oxo-2(lH)-phthalazinyl}-1-piperidinyl}acetyl]- (9CI) (CA INDEX NAME)

RN 449760-51-4 CAPLUS (N 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-54-7 CAPLUS '
CN Morpholine,
4-[[4-[445,8eR]-4-[3,4-diethoxyphenyl]-4e,5,8,8e-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-piperidinyl}scetyl]- (9CI) (CA INDEX NAME)

RN 449760-55-8 CAPLUS
CN 1-Piperazineethanamine,
4-[(485.8a8)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-0xo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl(9CI) (CA INDEX NAME)

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-56-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-[{4-(1,2,3-thiadiazol-4-yl)phenyl}methyl}-4-piperidinyl]-, (4aS,8aR)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-[[{4-[{4aS,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(lR)-phthalazinyl}-1-piperidinyl]acetyl]amino]-, ethylester (GCI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 5 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-58-1 CAPLUS
1-Piperidinectamide, 4-{{4as,8aR}-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}- (9CI) (CA INDEX RAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

(Continued)

FORMAT

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN

ACCESSION NUMBER:
DOCUMENT NUMBER:
141:406064
Composition comprising a PDE4 inhibitor and soluble human Type II interleukin-1 receptor (shuIL-1RII) for disease therapy
BATENT ASSIGNEE(S):
SOURCE:
DOCUMENT TYPE:
LANGUAGE:
PAMILY ACC. NUM. COUNT:
LANGUAGE:
PATENT INPORMATION:

DOCUMENT TYPE: LANGUAGE: PAMILY ACC. NUM. COUNT: PATENT INFORMATION:

MO 2004098606 A1 20041118 WO 2004-EP50749 20040510
M: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BR, BR, BM, BY, BZ, CA, CH, CD, CD, CD, CD, CD, CD, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MM, MM, MX, MZ, NA, NI, NO, NZ, CM, PG, PH, PL, PT, RC, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TH, TN, TR, TT, TZ, LA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZM, RM, EM, GM, GM, KE, LS, MM, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZM, ZM, AZ, EY, KG, KZ, MD, RU, TJ, TM, AT, EB, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BP, BJ, CP, CG, CI, CM, GA, GN, GO, GM, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO:

The invention relates to the combined administration of a PDE4 inhibitor and shull-IR II for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental. 449760-15-0 449760-16-1 449760-17-2 449760-15-0 449760-16-1 449760-17-2 449760-20-7 449760-21-0 449760-22-9 449760-22-0 449760-23-0 449760-23-0 449760-25-2 449760-25-0 449760-30-9 449760-31-6 449760-30-6 449760-30-9 449760-31-6 449760-31-6 449760-31-6 449760-31-6 49760-31-6

RN 449760-14-9 CAPLUS CN Piperidine, 4-{(445,847)-4-(3,4-diethoxyphenyl)-48,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalarinyl}-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-15-0 CAPLUS CN Piperidine, 4-{(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(H)-phthalazinyl)-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyll- (9Cl) (CA INDEX RAME)

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-[(445,881)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-19-4 CAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-22-9 CAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aR,8as)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

RN 449760-23-0 CAPLUS

N Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl)(9C1) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-20-7 CAPLUS
CN 1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-21-8 CAPLUS
CN 1-Piperidinecarboxanide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N-(1,1-dimethylethyl)- (9CI) (CA INDEX RAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-26-3 CAPLUS CN Morpholine, 4-[[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-0x0-2(1H)-phthalazinyl)-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

449760-29-6 CAPLUS 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2pyrimidinyl)-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
-(3,4-dimethoxyphenyl)-4e,5,8,8a-tetrahydro-2-[1-[1methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

RN 449760-35-4 CAPLUS CN Morpholine, 4-[[4-{(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-{(4aS,8aR)-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-(1-methylethyl)- {9CI} (CA INDEX NAME)

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

OMe OMe N B H

RN 449760-42-3 CAPLUS
2,3-Piperazinedione, 1-[[4-[[4aS,8aR]-4-[3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-0x0-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-47-8 CAPLUS
CN Piperidine,
4-[{4aS,8aR}-4-{1,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) INDEX NAME)

Absolute stereochemistry.

RN 449760-50-3 CAPLUS
CN Morpholine,
4-[[4-6,8aR]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-0x0-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2phenylethyl)-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

N 449760-48-9 CAPLUS
N 1(2H)-Phthalazinone, 2-{1-{2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl}-4piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-49-0 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4as,8aR)- (9CI) (CA

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-52-5 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3pyridinylmethyl)-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA INDEX NAME)

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(2pyridinylmethyl)-4-piperidinyl}-, (4eS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-54-7 CAPLUS CN Morpholine, 4-{{4-{44,8aR},4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl}- (9CI) (CA INDEX NAME)

RN 449760-55-8 CAPLUS
CN 1-Piperazineethanamine,
4-[(4-(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-0xo-2(1H)-phthalazinyl]-1-piperidinyl)acetyl}-N,N-dimethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-58-1 CAPLUS
1-Piperidineacetamide, 4-{{4aS,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT

FORMAT

THERE ARE 5 CITED REPERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L4 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-56-9 CAPLUS CN 1(3H)-Phthalazinone, 4-(3,4-dimethoxypheny)1-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiaddazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-{[[4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethylester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:995978 CAPLUS
DOCUMENT NUMBER: 141:460663
TITLE: Pharmaceutical composition comprising a PDE4 . inhibitor

and IL-1 trap for treatment of disease Barsig, Johannes Altane Pharma AG, Germany PCT Int. Appl., 24 pp. CODEN: PIXXD2 Patent English 1

INVENTOR (S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.						D	DATE			APPL	ICAT	DATE								
						+														
WO 2004098605				Al		2004	1118	1	WO 2	004-	EP50	747		2	0040	TE 040510 CA, CH, 3B, GD, KZ, LC, NA, NI, SL, SY, ZM, ZW ZW, AM, DE, DK, RO, SE, RRO, NE,				
	₩:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BΑ,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,			
		CN,	co,	CR,	CU.	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	PI,	GB,	GD,			
		GΕ,	GH,	GM,	HR.	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR.	KZ.	LC.			
		LK,	LR,	LS,	LT,	LU,	LV.	MA,	MD,	MG,	MK,	MIN.	MW,	MX.	MZ.	NA.	NI.			
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	sc.	SD.	SE,	SG,	SK,	SL,	SY,			
	RW:	BW,	GH,	GM,	KE,	LS,	MW,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,			
		AZ,	BY,	KG,	KZ.	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE.	DK.			
		EE,	ES,	PI,	FR,	GΒ,	GR,	ΗU,	IE.	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,			
		SI,	SK,	TR,	BF,	BJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,			
		SN,	TD,	TG																
ORITY	APP	LN.	inpo	. :						EP 2	003 -	1063	1	1	A 2	0030	512			

The invention relates to the combined administration of a PDE4 inhibitor and IL-1 Trap for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or interleukin-1 (IL-1) activity is detrimental. 449760-14-9 449760-15-0 449760-16-1 449760-17-2 449760-19-4 449760-17-2 449760-19-4 449760-20-7 449760-17-2 449760-19-4 449760-20-7 449760-18-4 449760-25-2 449760-21-0 449760-18-4 449760-18-2 449760-20-9 449760-18-4 449760-18-2 449760-18-4 449760-18-2 449

for treatment of disease)
RN 449760-14-9 CAPLUS
CN Piperidine,
4-[(445,848)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-15-0 CAPLUS
CN Piperidine,
4-[(445,848]-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalezinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-20-7 CAPLUS
1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-21-8 CAPIUS
1-Piperidinecarboxamide, 4-{{4aS,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalaxinyl}-N-(1,1-dimethylethyl)- (9CI) (CA INDEX RAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-[(4a5,8a7)-4-(3,-d-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl]-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-22-9 CAPLUS
1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N{1,1-dimethylethyl}-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

449760-23-0 CAPLUS
Piperidine, 4-[(485,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1cxo-2(1H)-phthalarinyl]-1-[{5-(dimethylamino)-1-naphthalenyl]sulfonyl](SCI) (CA INDEX NAME)

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued

IMe<sub>2</sub>

PAGE 2-A

PAGE 1-A

RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4s,5,8,8s-tetrshydro-2-[1-[1methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8s-tetrahydro-2-[1-(4pyridinylmethyl)-4-piperidinyl]-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-26-3 CAPLUS
CN Morpholine,
4-[{4-[(4aS,8aR)-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (CA INDEX NAME)

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

RN 449760-29-6 CAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno(2,3-d)pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalaxinome,
4-(3,4-dimethoxyphenyl)-4e,5,8,8e-tetrahydro-2-[1-{2pyrimidinyl}-4-piperidinyl}-, (4eS,8eR)- (9CI) (CA INDEX NAME)
Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[{4-[{48,8aR}}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-piperidinyl|carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-40-1 CAPLUS
1-Piperidinescetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-48-9 CAPLUS 1(2H)-Phthalazinone, 2-[1-{2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl}-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4eS,8aR)-(9Cl) (CA INDEX NAME)

RN 449760-49-0 CAPLUS
CN 1(2H)-Phthalaxinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[{2-oxo-2H-1-benzopyran-7-yl}methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-42-3 CAPLUS
2,3-Piperazinedione, 1-[{4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl)carbonyl}-4-ethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-47-8 CAPLUS
CN Piperidine,
4-[(4a5,8a7]-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-50-3 CAPLUS
CN Morpholine,
4-{[4-[(48,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyllacetyl]- (9CI) (CA INDEX NAME)

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-disentoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2phenylethyl)-4-piperidinyl]-, (4a5,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-52-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3pyridinylmethyl)-4-piperidinyl]-, (4eS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-56-9 CAPLUS 1(2H)-Phthalazinone, 3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

449760-57-0 CAPLUS
Benzoic acid, 4-{[[4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2|1H]-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester (9Cl) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-54-7 CAPLUS CN Morpholine, 4-{[4-{(48,8aR) -4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl|acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-55-8 CAPLUS
CN 1-Piperazineethanamine,
4-[(4-(468,8a8)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-0xo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-N,N-dimethyl(9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 7 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-58-1 CAPLUS
1-Piperidineactamide, 4-[(4e5,8aR)-4-(3,4-dimethoxyphenyl)-4e,5,8,8a-terrahydro-1-oxo-2(1H)-phthalazinyl]- (9Cl) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSMER 8 OF 22
ACCESSION NUMBER:
DOCUMENT NUMBER:
111:416024
COMPOSITION COMPTISING PDE4 inhibitor and a THFW antegorist
BATEST ASSIGNEE(s):
BOURCE:
DOCUMENT TYPE:
LANGUAGE:
PAMILY ACC. NUM. COUNT: 1

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PA	TENT	NO.			KIN	D	DATE			APPL	I CAT	ION	NO.		D	ATE	
	WO 2004098578																
WO						A2 20041118					WO 2004-EP50750						
WO	WO 2004098578				A3		2004	1229									
	W:	AE,	AG,	λL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
		CN,	co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	ΕĖ,	EG,	ES,	PI,	GB,	GD,
		GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚĔ,	KG.	KP,	KR,	KZ,	LC,
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MEN,	MW,	MX,	MZ,	NA,	NI,
		NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
		ŦJ,	TM,	TN,	TR,	TT,	TZ,	UA,	UG,	υs,	υz,	VC,	VN,	Yυ,	ZA,	ZM,	ZW
	RW:	BW,	GH,	GM,	ΚE,	LS,	MN,	MZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
		AZ,	BY,	KG,	KŻ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
		EE,	ES,	PI,	PR,	GB,	GR,	ΗU,	IE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,
		SI,	SK,	TR,	BP,	BJ,	CF,	CG.	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,
		SN,	TD,	TG													
PRIORIT	Y APP	LN.	INFO	. :						EP 2	003-	1059	3		A 2	0030	512

The invention relates to the combined administration of a PDE4 inhibitor and a TNPa antagonist selected from the group consisting of infliximab, adalimumab, cdp870 and cdp571 for the treatment of a disease in which phosphodiesterase 4 (PDE4) and/or tumor necrosis factor alpha (TNPa) activity is detrimental.
449760-14-9 449760-15-0 449760-16-1
449760-17-2 449760-19-4 449760-16-1
449760-21-8 449760-22-9 449760-22-0
449760-24-1 449760-22-9 449760-26-3
449760-24-1 449760-25-2 449760-30-9
449760-35-4 449760-40-1 449760-42-3
449760-50-3 449760-51-4 449760-52-5
449760-50-6 449760-51-4 449760-52-5
449760-50-6 449760-51-0 449760-55-8
449760-50-6 9449760-51-0 449760-58-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Usee) (pharmaceutical injections containing phosphodiesterase 4 inhibitors

in combination with TNPG antagonists for treatment of arthritis and other diseases)
RN 449760-14-9 CAPUUS
CN Piperidine,
4-[(485,888]-4-[3,4-disethoxyphenyl)-48,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-17-2 CAPLUS
1-Piperidinepentanoic acid,
(as,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl}-8-oxo-(9CI) (CA INDEX NAME)

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-[{4aS,8aR}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahytro-1-oxo-2{lH}-phthalazinyl}-N-{1,1-dimethylethyl}- (9CI) (CA-INDEX\_NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

RN 449760-15-0 CAPLUS CN Piperidine, 4-[(445,848)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-(methylaulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-20-7 CAPLUS
1-Piperidinecarboxamide, 4-{(4a5,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-21-8 CAPLUS
1-Piperidinecarboxamide, 4-[{4aS,8aR}-4-(3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CAINDEX NAME)

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-22-9 CAPLUS
1-Piperidinecarboxamide, 4-[(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

449760-23-0 CAPLUS
Piperidine, 4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-{[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4as,8aR)- (9CI) (CA INDEX NAME)

RN 449760-26-3 CAPLUS
CN Morpholine,
4-{[4-{[44.58.88].4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9C1) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-28-5 CAPLUS
1(2H)-Phthalazinone,
4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-{1methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

449760-29-6 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(2-

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN NAME) (Continued)

Absolute stereochemistry.

449760-42-3 CAPLUS
2,3-Piperazinedione, 1-[[4-[{4aS,8aR}]-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl-(SCI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-47-8 CAPLUS
CN Piperidine,
4-{(445,887)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSMER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) pyrimidinyl}-4-piperidinyl}-, (4as,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[[4-[(48,8aR) -4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (9CI) (CA INDEX

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-48-9 CAPLUS 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-49-0 CAPLUS
CN 1(2H)-Phthalazinone,
1(3.4-(inethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-3H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX INNEX)

Absolute stereochemistry.

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L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-50-3 CAPLUS

RN 49780-30-3 CM Morpholine, 4-[(4-[(485,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-piperidinyl]acetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2-phenylethyl)-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-52-5 CAPLUS CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-(2pyridinylmethyl)-4-piperidinyl]-, (4as,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-54-7 CAPLUS
CN Morpholine,
4-{{4-{4aS,8aR}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1oxo-2[HH-phthalazinyl]-1-piperidinyl]acetyl}- (9C1) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

L4 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-56-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[4-(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8eR)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-{[[4-[[465,8aR]-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethylester (9CI) (CA INDEX NAME)

ANSWER 8 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-58-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
| lymphoid cells in combination with differentiation inducers and agents
that increase cAMP levels or cAMP analogs)
RN 449760-14-9 CAPLUS
CN Piperidine,
4-[(445,888-1-4-{3,4-diethoxyphenyl}-48,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl}-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 449760-15-0 CAPLUS
CN Piperidine,
4-[(445,847)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9Cl) (CA INDEX NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:610086 CAPLUS
DOCUMENT NUMBER: 141:134069
TITLE: PDE inhibitors for the treatment of neoplasms of

PDES inhibitors for the treatment of neoplasms of lymphoid cells Hatzelmann, Armin; Tenor, Hermann; Gekeler, Volker; Sanders, Karl; Garattini, Enrico; Braunger, Juergen; Schudt, Christian Altana Pharma Ag, Germany PCT int. Appl., 78 pp. CODEN: PIXXD2 Patent INVENTOR (S) :

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

	PAT	ENT	NO.			KIN	D	DATE			APPL	ICAT	ION	NO.		D	ATE	
			· • • •				-							• • • •		-		
	WO	2004	0626	71		A2		2004	0729		WO 2	004-	EP19	6		2	0040	114
	WO	2004	0626	71		A3		2005	0127									
		w:	ΑE,	AG,	AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
			CN,	co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC.	EE.	EG.	ES,	PI,	GB,	GD,
			GE,	GH,	GM,	HR,	HU,	ID.	IL.	IN.	15.	JP.	KE.	KG.	KP.	KR,	KZ,	LC,
			LK,	LR,	LS.	LT.	LU,	LV.	MA,	MD.	MG.	MK.	MN.	MW.	MX.	MZ		
	ΑU	2004							0729								0040	114
	CA	2512	819			A1		2004	0729		CA 2	004 -	2512	819		2	0040	114
	EP	1587	7512			A2		2005	1026		EP 2	004-	7019	02		2	0040	114
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT.	LI,	LU.	NL,	SE,	MC.	PT.
			IE,	SI,	LT,	LV.	FI,	RO.	MK.	CY.	AL.	TR.	BG.	cz.	EE.	HU.	sĸ	
	J₽	2006	5153	67		T		2006	0525		JP 2	006-	5005	61		2	0040	114
	US	2006	1488	04		A1		2006	0706		US 2	005-	5420	88		2	0050	713
RIOR	ITY	API	LN.	INFO	. :		-				EP 2	003-	787			A 2	0030	114

WO 2004-EP196

OTHER SOURCE(S): MARPAT 141:134069

AB The invention relates to the use of certain PDE4 inhibitors alone or in combination with one or more differentiation inducing agents and/or an agent effective in raising intracellular concens. of cAMP or a stable analog of cAMP in the preparation of pharmaceutical compns. for the treatment of neoplasms of lymphoid cells.

IT 449760-14-9 449760-15-0 449760-16-1 449760-17-2 449760-18-1 449760-17-2 449760-18-0 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 449760-18-1 549760-18-1 449760-18-1 549760-18-1 449760-18-1 559602-01-1 596102-07-7 596102-09-1 596102-07-1

596102-09-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (phosphodiesterase 4 (PDE4) inhibitors for treatment of neoplasms of

ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-[(445,887)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-8-oxo- (9CI) {CA INDEX NAME}

Absolute stereochemistry.

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-{{4aS,8aR}-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2{1H}-phthalazinyl}-N-{1,1-dimethylethyl}- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-20-7 CAPLUS
1-Piperidinecarboxamide, 4-{(4as,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-terrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-21-8 CAPLUS
1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CAIMDEX (NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4s,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME) Absolute stereochemistry.

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

449760-22-9 CAPLUS 1-Piperidinecarboxamide, 4-{{4aR,8aS}-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4s,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

449760-23-0 CAPLUS
Piperidine, 4-[(488,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(SCI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-{4pyridinylmethyl}-4-piperidinyl]-, (4eS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-26-1 CAPLUS
CN Morpholine,
4-{[4-{(48,88R)-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl}-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN (Continued No. 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4e,5,8,8a-tetrahydro-2-(1-(2-pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME) (Continued)

Absolute stereochemistry.

RN 449760-15-4 CAPLUS
CN Morpholine,
4-[[4-[(48,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

449760-40-1 CAPIUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (9CI) (CA INDEX MAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

449760-29-6 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno(2,3-d)pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

449760-30-9 CAPLUS

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

449760-42-3 CAPLUS 2,3-Piperazinedione, 1-{[4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl}carbonyl]-4-ethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-47-8 CAPLUS CN Piperidine, 4-[(4as, 5as]-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

449760-48-9 CAPLUS
1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4piperidinyl]-4-(3,-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)(9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-49-0 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxypheny)-4a,5,8,8a-tetrahydro-2-[1-[(2-oxo-2H-1-benzopyran-7-yl)methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

RN 449760-52-5 CAPLUS
CN 1(2H)-Phthblazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN INDEX NAME)

Absolute stereochemistry.

RN 449760-50-3 CAPLUS
CN Morpholine,
4-[[4-[(48, 8aR) -4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl)-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2-phenylethyl}-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA INDEX NAME)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-56-9 CAPLUS
1(2H)-Phthalazinone,
3,4-dimethoxyphenyll-4a,5,8,8a-tetrahydro-2-[1-[[4(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI)
(CA INDEX NAME)

449760-57-0 CAPLUS
Benzoic scid, 4-{[[4-{[4as,8aR]-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(18]-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethylester (9CI) (CA INDEX NAME)

449760-58-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 596102-01-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methylethyl)-4-piperidinyl]- (9Cl) (CA INDEX NAME)

ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

L4 ANSWER 9 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 596102-07-7 CAPLUS
CN Piperidine,
4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(4-morpholinylacetyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 596102-09-9 CAPLUS
CN Piperidine,
4-[(4aS,8aR]-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl)-1-[[4-[2-(dimethylamino)ethyl]-1-piperazinyl)acetyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSMER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
DOCUMENT NUMBER:
111LE:
110:217552
Preparation of pyrrolidinedione substituted piperidine-phthalazones as cyclic nucleotide phosphodicaterase-4 (PD84) inhibitors
Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Kley, Hans-Peter; Christicans, Johannes A. M.; Menge, Wiro M. P. B.; Sterk, Geert Jan
Altana Pharma A.-G., Germany
POT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE:
LANGUAGE:
PAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
2

PAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO.																	
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WO	2004	0184	57		A1		2004	0304	1	WQ 2	003-	EP86	75		2	0030	806
WO	2004	0184	57		AB		2004	0506									
	W:	AE,	AL,	AU,	BA,	BR,	CA,	CN,	co,	DZ,	EC,	GE,	HR,	ID,	IL,	IN,	IS,
		JP,	KR,	LT,	LV.	MA,	MK,	MX,	NO,	NZ,	PH,	PL,	SG,	TN,	UA,	US,	VN,
		YU,	ZA,	ZW													•
	RW:	AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,
		DK,	EE,	ES,	FI,	PR,	GB,	GR,	HU,	IE,	IT,	LU,	MC.	NL,	PT,	RO.	SE.
		SI,	SK,	TR													
CA	2494	613			A1		2004	0304		CA 2	003-	2494	613		2	0030	806
AU	2003	2585	76		A1		2004	0311	- 1	AŲ 2	003-	2585	76		2	0030	806
EP	1537	100			Al		2005	0608		EP 2	003-	7922	57		2	0030	806
	R:	AT,	BE,	CH,	DE,	DK,	ES.	FR,	GB,	GR,	IT,	LI.	LU,	NL,	SE,	MC,	PT.
		IE,	SI,	LT.	LV.	PI,	RO,	MK,	CY,	AL,	TR.	BG.	CZ.	EE.	HU,	SK	
BR	2003	0133	30		Α		2005	0614		BR 2	003-	1333	0		2	0030	806
CN	1671	695			Α		2005	0921		CN 2	003-	8185	20		2	0030	806
JP	2006	5003	70		T		2006	0105		JP 2	004-	5300	86		2	0030	806
IN	2005	MNOO	028		A		2005	0218		IN 2	005-	MN28			2	0050	112
US	2006	1608	13		A1		2006	0720		US 2	005-	5234	12		2	0051	107
PRIORIT	Y APP	LN.	INFO	. :						EP 2	002-	1797	_			0020	

WO 2003-EP8675 OTHER SOURCE(S): MARPAT 140:217652

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

1-(4-Piperidinyl)-4a,5,8,8a-tetrahydro-1H-phthalazin-1-one compds. of formula (I) (R1 and R2 are both H or together form an addnl. bond; R3 = a Ph derivative of formulas Q or Q1; R4 = C1-4 alkoxy or C1-4 alkoxy which

W 20030806

completely or predominantly substituted by fluorine; R5 = C1-4 alkoxy, C3-7 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R6 = C1-4 alkoxy or C1-4 alkoxy which is completely or predominantly substituted by fluorine; wherein R7

C1-4 alkyl; R8 = H, C1-4 alkyl; or R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked

02/09/2007

L4 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulfur atom; R9 = CO(CH2)n-R10; wherein R10 = 2.5-dioxopyrrolidin-1-y1; n = an integer of 1-4) and the salts of these compds. These compds are useful in the prepn. of pharmaceutical compns. for the treatment of an illness treatable by the administration of a PDE4 inhibitor, in particular airway disorders. Thus,
1-[2-[4-[(4eS,8aR)-4-(3,4-Dimethoxypheny1)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]piperidin-1-yl]-2-cxoethyl]pyrrolidin-2,5-dione >. Thus, a mixt. of 1 g (4aS,8aR)-2-[1-(2-Chlorocthanoyl)piperidin-4-yl]-4-[3,4-dimethoxypheny1)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one, 0.4 g succinimide, 1 g potassium

potassium carbonate in 20 mL DMP was stirred for 18 h at room temp. to give, after workup and silics gel chromatog, and crystn. from EtOAc, 1-[2-[4-[4as],8aR].4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthelazin-2-yl.]piperidin-1-yl]-2-oxoethyl]pyrolidine-2,5-dione (II).

showed -logic50(mol/L) of 10.66 against PDE4.
380226-97-1P, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-piperidin-4-yl4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride
380227-13-4P, (4AS,8aR)-4-(3,4-Diethoxyphenyl)-2-piperidin-4-yl4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride
666735-57-5P 666735-56-0-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of pyrrolidinedione substituted piperidine-phthalazones as cyclic nucleotide phosphodiesterase-4

inhibitors for treating airway diseases)
380226-97-1 CAPLUS
1(2H)-Phhalezinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666735-60-0 CAPLUS
CN 1(2H)-Phthalazinone,
(-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride,
(4aR,8a5)-rel(SCI) (CA INDEX NAME)

Relative stereochemistry.

● HC1

666735-56-4P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES cs; (preparation of pyrrolidinedione substituted piperidine-phthalazones L4 ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

● HC1

380227-13-4 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)-(9CI) (CA INDEX NAME)

666735-57-5 CAPLUS
Piperidine, 1-(chloroacetyl)-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

ANSWER 10 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) cyclic nucleotide phosphodiesterase-4 (PDE4) inhibitors for treating airway diseases) 666735-56-4 CAPLUS Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(INI)-phthelazinyl]-1-[(2,5-dioxo-1-pyrrolidinyl)acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

## 10/523,111

## Page 43

L4 ANSMER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:
DOCUMENT NUMBER:
10:217651
INVENTOR(S):

INVENTOR(S):

ACTION PATENT ASSIGNEE(S):
SOURCE:
DOCUMENT TYPE:

CAPLUS COPYRIGHT 2007 ACS on STN
2004:182864 CAPLUS
10:217651
Preparation of piperidinylpyridazinones as inhibitors of phosphodiesterase PDS4 or PDS3/4 inhibitors.
Action of phosphodiesterase PDS4 or PDS3/4 inhibitors.

DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

			···														
PA	TENT	NO.			KIN	D	DATE			APPI	LICAT	ION	NO.		D.	ATE	
						_									-		
WO	2004	0184	51		A1		2004	0304		WO 2	2003 -	EP86	77		2	0030	806
WO	2004	0184	51		A8		2004	0506									
	W:	AE,	AL,	AU,	BA,	BR,	CA,	CN,	co,	DZ,	EC,	GE,	HR,	ID,	IL,	IN,	IS,
		JP,	KR,	LT,	LV,	MA,	MK,	MX,	NO,	NZ,	PH,	PL,	SG,	TN,	UA,	US,	VN,
		YU.	ZA.	ZW													
	RW:	AM.	AZ.	BY.	KG.	KZ.	MD,	RU.	TJ,	TM.	AT.	BE.	BG.	CH.	CY.	CZ.	DE.
		DK,	EE.	ES,	FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,
		SI,	SK,	TR													
CA	2494	650	-		A1		2004	0304		CA 2	2003-	2494	650		2	0030	806
AU	2003	2516	93		Al		2004	0311		AU 2	2003 -	2516	93		2	0030	806
EP	1556	369			Al		2005	0727		EP 2	2003 -	7922	59		2	0030	806
											IT.						
		IE.	SI.	LT.	LV,	FI,	RO,	MK,	CY,	AL,	TR.	BG.	CZ,	EE.	HU.	SK	
J₽	2005	5381	38		T		2005	1215		JP 2	2004 -	5300	88		2	0030	806
ບຣ	2006	1670	01		A1		2006	0727		vs_2	2005-	5221			2	0050	203
PRIORIT										ÉP :	2002 -	1797	6		A 2	0020	810
										wo a	2003 -	EP86	77		w 2	0030	806

OTHER SOURCE(S): MARPAT 140:217651

Title compds. {I; R1, R2 = H, alkyl; R3 = Q1, Q2; R4 = (fluoro)alkoxy;

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007-ACS on STN (Continued)

666750-57-8 CAPLUS
3(2H)-Pyridazinone,
4-dimethoxyphenyl)-4,5-dihydro-2-(4-piperidinyl), monohydrochloride (9CI) (CA INDEX NAME)

● HCl

RN 666750-58-9 CAPLUS
CN 3(2H)-Pyridazinone,
6-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4,5-dihydro-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

● HC1

RN 666750-59-0 CAPLUS CN Piperidine, 1-acetyl-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-4-methyl-6-oxo-1(4H)-pyridazinyl)- (9CI) (CA INDEX NAME)

L4 ANSMER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

R6 = cycloalkoxy, cycloalkylmethoxy, (floorolalkoxy, R7 = alkyl, R8 = H,
alkyl, R7R8 = atoma to form a 5-7 membered ring optionally interrupted by
O, S; R9 = alkyl, SO2R10, COR13, aryl, etc.; R10 = alkyl,
S-dimethylaminonaphthalen-1-yl, thienyl, NR16R17, (substituted) Ph, etc.;
R13 = alkyl, carboxyalkyl, Ph, pyridyl, NR16R17, etc.; R16 = H, alkyl,
cycloalkylmethyl, (substituted) Ph; R17 = alkyl, cycloalkylmethyl, (substituted) Ph; R17 = alkyl, cycloalkylmethyl, (substituted) Ph; R17 = alkyl, cycloalkyl,
cycloalkylmethyl, (substituted) Ph; NR16R17, etc.; R16 = H, alkyl,
cycloalkylmethyl, 1-piperidinyl, 1-hexabydroacypinyl, (substituted)
piperazinyl), were prepd. Thue, piperidin-4-ylhydrazine dihydrochloride
(prepn. given), 4-(3, 4-dimethoxyphenyl)-3-methyl-4-oxobutyric acid, and
EtlN were refluxed 18 h in PrOH to give
6-(3, 4-dimethoxyphenyl)-5-methyl-2-piperidin-4-yl-4,5-dihydro-3H-pyridazin-3-one hydrochloride. I inhibited
PDE4 with -log ICSO = 7,17-8.39.
PDE6-56-57-6-(3,4-Dimethoxyphenyl)-5-methyl-2-piperidin-4-yl4,5-dihydro-3H-pyridazin-3-one hydrochloride 666750-58-9P 66750-61-9P 666750-62-5P 666750-60-3P
666750-61-P 666750-62-5P 666750-60-3P
666750-61-P 666750-74-9P 666750-72-7P
666750-70-P 666750-74-9P 666750-72-7P
666750-76-1P 666750-74-9P 666750-73-3P
666750-76-1P 666750-74-9P 666750-78-3P
666750-82-9P 666750-74-9P 666750-78-3P
666750-82-9P 666750-80-7P 666750-78-1P
666750-92-9P 666750-80-7P 666750-78-1P
666750-92-9P 666750-78-9P
666750-92-9P 666750-80-9P
666750-85-9P 666750-78-9P
666750-85-9P 666750-78-9P
666750-85-9P 666750-78-9P
666750-85-9P 666750-86-1P
666750-85-7 Abulls

(Preparation of piperidinylpyridazinones as phosphodies

/4
inhibitors)
666750-56-7 CAPLUS
3 (2H) -Pyridazinone, 6-(3,4-dimethoxyphenyl)-4,5-dihydro-5-methyl-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

HC1

ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

666750-60-3 CAPLUS
Morpholine, 4-[[4-[3-(3.4-dimethoxyphenyl)-5,6-dihydro-4-methyl-6-oxo-1(4H)-pyridazinyl]-1-piperidinyl]carbonyll- (9CI) (CA INDEX NAME)

CAPLUS

3(2H)-Pyridazinone, 6-(3,4-dimethoxyphenyl)-4,5-dihydro-5-methyl-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

●2 HC1

666750-62-5 CAPLUS
2,3-Pipersrinedione, 1-[[4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)-1-piperidinyl]carbonyl]-4-ethyl- (9Cl) (CA INDEX

## 10/523,111

## Page 44

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

Med No Control of Cont

RN 666750-63-6 CAPLUS

Piperazine, 1-[[4-[3-{3,4-dimethoxyphenyl}]-5,6-dihydro-6-oxo-1(4H)pyridazinyl)-1-piperidinyl]carbonyl]-4-methyl-, monohydrochloride (9CI)
(CA INDEX NAME)

● HC

RN 666750-64-7 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl]-1-[[S-(dimethylamino)-1-naphthalenyl]sulfonyl]- (9CI) (CA
INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666750-67-0 CAPLUS
CN Piperidine, 4-{3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl}-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

RN 666750-68-1 CAPLUS
CN Piperidine, 1-[(4-chlorophenyl)sulfonyl]-4-[3-(3,4-dimethoxyphenyl)-5,6-dhydro-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)

RN 666750-69-2 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridaxinyl)-1-([bhenylmethyl)sulfonyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666750-65-8 CAPLUS
CN Morpholine, 4-[[4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl}-1-piperidinyl]acetyl]-, monohydrochloride (9CI) (CA INDEX
NAME)

● HCI

RN 666750-66-9 CAPLUS
CN Piperidine, 4-{3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridszinyl}-1-[(4-methylphenyl)aulfonyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666750-70-S CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl|-1-[(4-methoxyphenyl)aulfonyl)- [9CI] (CA INDEX NAME)

RN 666750-71-6 CAPLUS

Piperidine, 4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]--(phenyleulfonyl)- (SCI) (CA INDEX NAME)

RN 666750-72-7 CAPLUS
Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl)-1-[(2,5-dimethoxyphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

RN 666750-73-8 CAPLUS
CN Piperidine, 1-[(2-cyanophenyl)sulfonyl]-4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)- (9CI) (CA INDEX NAME)

RN 666750-74-9 CAPLUS
CN Piperidine, 4-{2-{3,4-dimethoxyphenyl}}-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)

RN 666750-75-0 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)-1-[(2-fluorophenyl)sulfonyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666750-79-4 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl]-1-(3-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

RN 666750-80-7 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)-1-(2,4,6-trichlorobenzoyl)- (9CI) (CA INDEX NAME)

RN 666750-81-8 CAPLUS
CN 1-Piperidinecarboxamide, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo1(4H)-pyridsxinyll-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666750-76-1 CAPLUS
CN Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl)-1-[[2-(trifluoromethoxy)phenyl]sulfonyl)- (9CI) (CA INDEX NAME)

RN 666750-77-2 CAPLUS
CN 1-Piperidinesulfonamide, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)-N,N-dimethyl- (9CI) (CA INDEX NAME)

RN 666750-78-3 CAPLUS
CN Piperidine, 1-benzoyl-4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 666750-82-9 CAPLUS
CN 1-Piperidineacetamide,
4-[3-(3,4-dimethoxy)henyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl]-N,N-dimethyl-, monohydrochloride (9CI) (CA INDEX NAME)

• HC1

RN 666750-83-0 CAPLUS
CN Piperazine, 1-[[4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-piperidinyl]acetyl]-4-methyl-, dihydrochloride (9CI) (CA INDEX NAME)

●2 HC1

666750-84-1 CAPLUS
Piperidine, 4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridazinyl]-1-[[4-(4-pyridinyl)-1-piperazinyl]acetyl]-, dihydrochloride
(9CI) (CA INDEX NAME)

●2 HCl

666750-85-2 CAPLUS
Piperidine, 4-(3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)pyridszinyl]-1-[(4-(2-methoxyphenyl)-1-piperazinyl]acetyl]-,
dihydrochloride (9C1) (CA INDEX RAME)

ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

REFERENCE COUNT:

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

(Continued)

FORMAT

L4 ANSWER 11 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

●2 HC1

666750-86-3 CAPLUS
Piperidine, 4-[3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]-1-[4-(diphenylmethyl)-1-piperazinyl)acetyl]-,
dihydrochloride (9CI) (CA INDEX NAME)

666750-88-5P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (preparation of piperidinylpyridazinones as phosphodiesterase PDE4 or

PDE3/4
inhibitors)
RN 666750-88-5 CAPLUS
CN Piperidine,
1-(chloroacetyl)-4-{3-(3,4-dimethoxyphenyl)-5,6-dihydro-6-oxo1(4H)-pyridazinyl)- (9CI) (CA INDEX NAME)

L4 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER:
DOCUMENT NUMBER:
11TLE:
1NVENTOR(S):
1NVENTOR(S):
2004:182863 CAPLUS
2004:18

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE

MO 2004012450 A1 20040304 W0 2003-EP8676 20030806

N: AB, AL, AU, BA, BR, CA, CN, CO, DZ, EC, GB, HR, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL, SG, TN, UA, US, VN, YU, ZA, ZN

RM: AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BS, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

CA 2494643 A1 20040304 CA 2003-2494643 20030806

AU 2003260371 A1 20040311 AU 2003-260371 20030806

EP 1542987 A1 20050622 EP 2003-792258 20030806

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
JP 2005538137 T 20051215 JP 2005-530317 20030806

US 2006166995 A1 20060727 US 2005-523110 20050203

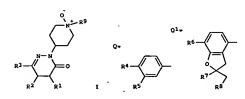
PRIORITY APPLN. INFO.:

WO 2003-EP8676

W 20030806

OTHER SOURCE(S):

MARPAT 140:235730



The 1,2-dihydro-2-(1-oxidopiperidin-4-yl)phthalazin-2-one derivs. (I; R1, R2 = H, C1-4 alkyl; or R1 and R2 together and with inclusion of the two 02/09/2007

ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) carbon atoms, to which they are bonded, form a group selected from cyclohexane-1,2-diyl or 4-cyclohexane-1,2-diyl; R3 = a Ph deriv. of formulae Q or Q1; R4 = C1-4 alkoxy or C1-4 alkoxy which is completely or predominantly substituted by fluorine; R5 = C1-8 alkoxy, C3-7 loalkoxy, C3-7 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R6 = C1-4 alkoxy, C3-5 cycloalkoxy, C3-5 cycloalkylmethoxy, C1-4 alkoxy which is completely or predominantly substituted by fluorine; R7 = C1-4 alkyl; R8 = H, C1-4 alkyl; or wherein R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulfur atom; R9 = (CH2)mSORRIO, (CH2)nCORII, -(CH2)p-Z-(CH2)q-R14; wherein R10, R11 = N(R12)R13; R12, R13 = H, C1-7 alkyl, C3-7 cycloalkyl, C3-7 cycloalkylmethyl; or NR12R13 together forms a 4-morpholinyl-, 1-piperidinyl- or a 1-hexahydroazepinyl ring; Z = a d,

O, CO, CONH, NHCO, SO2; R14 = H, OH, C1-4 alkoxy, hydroxy-C2-4 alkoxy, C1-4 alkoxy-C1-4 alkoxy, C1-4 alkoxy, C1-4 alkoxy-C1-4 alkoxy-C1-4

Dimethoxy)phenyl]-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]piperidin-1-yl-2H-acetamide hydrochloride in 100 mL CH2Cl2 was washed with aq. satd.

NaHCO3 soln., dried over anhyd. MgSO4, cooled to 0°, treated with 0.6 g 3-chloroperbenzoic acid (70% purity), and stirred for 60 min to give, after workup and silca gel chromatog. and crystn. from EtOA; 2-(4-[(485,8aR]-4-[3,4-bimethoxyphenyl]-1-oxo-4a,5,8,8a-tet-ahydro-H-phthalazin-2-yl]-1-oxypiperidin-1-yl]acetamide [II]. II and 2-(4-[(485,8aR]-4-[3,4-bimethoxyphenyl]-1-oxo-4a,5,8,8a-tetrahydro-H-phthalazin-2-yl]-1-oxypiperidin-1-yl]-N-isopropylacetamide showed IC50

phthalazin-2-yij-1-oxypiperidin-1-yij-N-180ptopyiacetamide whowes
-pogicSo (mol/L) of 8.31 and 9.3, resp., against PDE4.

IT 380226-97-19 380227-31-4P, (48,8 aR) -4-(3,4Diethoxyphenyl)-2-piperidin-4-yi-4a, 5,8,8 a-tetrahydro-2H-phthalazin-1-one
hydrochloride 449760-40-1P 449760-44-5P 666735-60-0P 666748-55-6P 666748-56-7P

(4AS, 8aR)-4-(3,4-Dimethoxyphenyl)-2-piperidin-4-yl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one hydrochloride RL: RCT (Reactant): SFN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (Intermediate; preparation of piperidine N-oxide derivs. as phosphodiesterase 4 (PDE4) inhibitors for treating airway disorders) RN 380226-97-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-44-5 CAPLUS 1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-, monohydrochloride (9CI) (CA INDEX NAMS)

Absolute stereochemistry

● HCl

RN 666735-60-0 CAPLUS
CN 1(2H)-Phthalaxinone,
4(2,3-dimydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride,
(4aR,8aS)-rel[9C1] (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

● HCl

380227-13-4 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HCl

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)- (9CI) (CA INDEX

ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

• HC1

RN 666748-55-6 CAPLUS
CN 1-Piperidineacetamide,
4-(14a5,887)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8ahexahydro-1-oxo-2(1H)-phthalazinyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

666748-56-7 CAPLUS
1(2H)-Phthalazinone,
4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2-(4piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

02/09/2007

● HCl

666854-35-9P 666854-37-1P 666854-40-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES

(preparation of piperidine N-oxide derivs. as phosphodiesterase 4 (PDE4)

inhibitors for treating airway disorders)
666854-35-9 CAPLUS
1-Piperidineacetamide, 4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a
tetrahydro-1-oxo-2(1H)-phthalazinyl]-, 1-oxide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

666854-37-1 CAPLUS

L4 ANSMER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN (CON CN 1-Piperidineacetamide, 4-[(4a5, 8a7]-4-(3, 4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME) (Continued)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 10 CITED REFERENCES AVAILABLE FOR

RECORD. ALL CITATIONS AVAILABLE IN THE RE

ANSWER 12 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
1-Piperidineacetamide, 4-[(4eS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1-methylethyl)-, 1-oxide (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

666854-40-6 CAPLUS

CN 1-Piperidineacetamide, 4-[(4as, 8aR)-4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-1-xo-2(1H)-phthalazinyl]-, 1-oxide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 666748-54-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; preparation of piperidine N-oxide derivs. as
phosphodiesterase 4
(PDE4) inhibitors for treating airway disorders)
RN 666748-54-5 CAPLUS

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2004:182862 CAPLUS DOCUMENT NUMBER: 140:217665

Preparation of piperidinylphthalazinone derivatives TITLE:

INVENTOR(S):

PDE4 inhibitors
Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard;
Kley, Hans-Peter; Christiaans, Johannes A. M.; Menge,
Wiro M. P. B.; Sterk, Geert Jan; Weinbrenner, Steffen
Altana Pharma A.-G., Germany
PCT Int. Appl., 48 pp.
CODEN: PIXXD2
Patent
English
1

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE:

PAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT	KIN	D	DATE		APPLICATION NO.						DATE				
				-						<b>-</b>			-		
WO 2004	018449		A1		2004	0304	1	WO 2	003-	EP86	73		2	0030	806
WO 2004	018449		A8		2004	0506									
W:	AE, AL,	AU,	BA.	BR.	CA.	CN.	co.	DZ.	EC.	GE.	HR.	ID.	IL.	IN.	IS,
	JP, KR,														
	YU, ZA,	ZW													
RW:	AM, AZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ.	DE,
	DK, EE,	ES.	PI,	FR,	GB,	GR,	ΗU,	IE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,
	SI, SK,	TR													
AU 2003	255376		A1		2004	0311		AU 2	003-	2553	76		2	0030	806
PRIORITY APP	LN. INFO						1	EP 2	002-	1797	9		A 2	0020	810
							1	WO 2	003-	EP86	73	,	W 2	0030	806

OTHER SOURCE(S): MARPAT 140:217665

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

The title compound I [R1, R2 = H or together form an addnl. bond; R3 = benzene derivative Q1 or Q2; R4 = (substituted)arylsulfonyl; R5 = alkoxy

polyfluoroalkyoxy; R6, R7 = (cyclo)alkoxy, cycloalkylmethoxy, or polyfluoroalkyoxy; R8 = alkyl; R9 = H or alkyl; or R7 and R8 together

with the 2 intervening C atoms form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by 0 or 5] were prepared as PDE4 inhibitors. Thus, reaction of (4s8,8aR)-4-(14,4-dimethoxyphenyl)-2-piperidin-4-yl-4a,5,8.8a-tetrahydro-2H-phthalazin-1-ome hydrochloride (preparation given) with naphthalane-1-sulfonyl chloride gave compound The

The prepared compds. inhibited PDE4 with -log(IC50) ≥ 8.8.
666737-07-1P 666737-09-3P 666737-10-6P
666737-11-7P 666737-12-8P 666737-13-9P
666737-14-0P 666737-15-1P 666737-16-2P
666737-12-3P 666737-18-4P 666737-19-5P
666737-30-8P 666737-21-9P 666737-22-0P
666737-32-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU

ANSMER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS On STN (Continued) (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of piperidinylphthalazinone derivs. as PDE4 inhibitors) 666737-07-1 CAPLUS Piperidine, 4-[(485,88R)-4-(3,4-dimethoxyphenyl)-48,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-(1-naphthalenylsulfonyl)- (9CI) (CA INDEX)

Absolute stereochemistry.

666737-09-3 CAPLUS
Piperidine, 4-[{4aS,8aR}-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-{{phenylmethyl}sulfonyl}- (9CI) (CA INDEX

Absolute stereochemistry.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

666737-12-8 CAPLUS
Piperidine, 4-([485,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,88-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(2-thienylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

666737-13-9 CAPLUS
Piperidine, 4-{(4aS,8aR)-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-{(3,5-dimethyl-4-isoxazolyl)sulfonyl}- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

666737-10-6 CAPLUS
Piperidine, 1-[(5-chloro-1,3-dimethyl-1H-pyrazol-4-yl)sulfonyl]-4[(4s5,8s7,4-4-(3,4-dimethoxyphenyl)-4e,5,8,8s-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

666737-11-7 CAPLUS
Piperidine, 4-(448,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-(8-quinolinylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

666737-14-0 CAPLUS
Piperidine, 1-[(5-chloro-2-thienyl)sulfonyl]-4-[(4eS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

666737-15-1 CAPLUS
Piperidine, 4-{(4aS,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-cxo-2(1H)-phthalazinyl}-1-{[2-(trifluoromethoxy)phenyl}sulfonyl}- (9CI)
(CA INDEX NAME)

666737-16-2 CAPLUS
3-Thiophenecarboxylic acid, 5-[[4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(iH)-phthalazinyl}-1-piperidinyl]sulfonyl]-4-methoxy-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

666737-17-3 CAPLUS
Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(IN)-phthalazinyl]-1-[[4-(phenylsulfonyl)-2-thienyl]sulfonyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

666737-20-8 CAPLUS
Piperidine, 1-[(4,5-dichloro-2-thienyl)sulfonyl}-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

RN 666737-21-9 CAPLUS
CN Piperidine,
1-[(5-chloro-3-methylbenzo[b]thien-2-yl)sulfonyl]-4-[(4aS,8aR)4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

666737-18-4 CAPLUS
Benzamide, N-[[5-{[4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-piperidinyl]sulfonyl]-2-thienyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

666737-19-5 CAPLUS
Piperidine, 4-(468,8eR)-4-(3,4-dimethoxyphenyl)-4e,5,8,8e-tetrshydro-1-oxo-2(1H)-phthalazinyl]-1-[{5-(3-isoxazolyl)-2-thienyl]sulfonyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

666737-22-0 CAPLUS
Piperidine, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-[[5-(2-pyridinyl)-2-thienyl]sulfonyl]- (9CI)
(CA INDEX NAME)

666737-23-1 CAPLUS
Piperidine, 4-[(4eS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-[(4-(trifluoromethoxy)phenyl]sulfonyl]- (9CI)
(CA INDEX NAME)

380226-97-1P 380227-13-4P 666735-60-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(preparation of piperidinylphthalazinone derivs. as PDE4 inhibitors)
380226-97-1 CAPLUS
12H1-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HC1

. 380227-13-4 CAPLUS 1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-

ANSWER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

REFERENCE COUNT:

THERE ARE 13 CITED REFERENCES AVAILABLE FOR

FORMAT

RECORD. ALL CITATIONS AVAILABLE IN THE RE

ANSMER 13 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 666735-60-0 CAPLUS
CN 1(2H)-Phthalazinone,
4-(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride,
(4aR,8aS)-rel(9CI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN
ACCESSION NUMBER: 2004:182711 CAPLUS
DOCUMENT NUMBER: 140:235729
TITLS: Preparation of piperidine-substituted pyridazones and phthe lazones as PDE4 inhibitors
Sterk, Geert Jan; Hatzelmann, Armin; Marx, Degenhard; Kley, Hans-Peter; Menge, Wiro M. P. B.
Altana Pharma A.-G., Germany
POT INTERT TYPE.

DOCUMENT TYPE.

CODEN: PIXMOZ

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

				APPLICATION NO.					
WO 2004	017974	. A1	20040304	WO 2003-EP8724	20030806				
W:	AE, AL,	AU, BA,	BR, CA, CN,	CO, DZ, EC, GE, HR,	ID, IL, IN, IS,				
	JP, KR,	LT, LV,	MA, MK, MX,	NO, NZ, PH, PL, SG,	TN, UA, US, VN,				
	YU, ZA,	ZW							
RW:	AM, AZ,	BY, KG,	KZ, MD, RU,	TJ, TM, AT, BE, BG,	CH, CY, CZ, DE.				
	DK, EE,	ES, PI,	FR, GB, GR,	HU, IR, IT, LU, MC,	NL. PT. RO. SE.				
	SI, SK,	TR							
CA 2494	634	A1	20040304	CA 2003-2494634	20030806				
AU 2003	260376	A1	20040311	AU 2003-260376	20030806				
EP 1556	049	A1	20050727	EP 2003-792267	20030806				
R:	AT, BE,	CH, DE,	DK, ES, FR,	GB, GR, IT, LI, LU,	NL, SE, MC, PT,				
	IE, SI,	LT, LV.	FI, RO, MK,	CY, AL, TR, BG, CZ,	EE, HU, SK				
JP 2005	538140	T	20051215	JP 2004-530096	20030806				
US 2006	094710	A1	20060504	US 2005-523111	20051003				
PRIORITY APP	LN. INFO	. :		EP 2002-17977	A 20020810				
				WO 2003-EP8724	W 20030806				

OTHER SOURCE(S): MARPAT 140:235729

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

Title compds. I [R1-2 = H, alkyl, etc.; R3 = substituted Ph, etc.; R9 = naphthyl, pyrazinyl, pyridazinyl, etc.] are prepared For instance,

(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride (preparation given) is reacted with methanesulfonylacetic acid (CH2Cl2, Et3N) to give II. Compds. of the invention have plCSO ≥ for the PDE4 receptor. I are useful for the treatment of sirway disorders.

IT 666851-01-0P, (4AS,8aR)-2-{1-{3-(2-aminoethanesulfonyl)propanoyl)p

iperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-

1-one
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); TRU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (preparation of piperidine-substituted pyridazones and phthalazones

as PDE4 02/09/2007

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) inhibitors)
666851-01-0 CAPLUS
Piperidine,
-[{2-aminoethyl)sulfonyl}-1-oxopropyl]-4-[{4aS,8aR}-4-{3,4-dimethoxyhenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}- (9CI)
(CA INDEX NAME)

IT 380227-17-8P, (4AS,8aR)-2-[1-[3-((2-Aminoethyl)sulfanyl)propanoyl]

1,2-dihydroquinolin-6-yl)oxy]butanoyl]piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one 666851-07-6P, (4AS,8aR)-2-[1-[2-(2-Aminoethoxy)ethyl]piperidin-4-yl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one dihydrochloride 666851-10-1P, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-methoxyethyl)piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride 666851-12-3P, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-methyl)piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride 666851-13-6P, (4AS,8aR)-4-(3,4-

Dimethoxyphenyl) -2-{1-{2-(methanesulfonyl)ethyl)piperidin-4-yl]-4a,5,8,8a-

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) tetrahydro-2H-phthalazin-1-one hydrochloride 666851-17-8P,

(4AS, 8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-[2-(2-hydroxyethoxy)ethyl]piperidin-4-yl]-4a.5,8,8a-tetrahydro-2H-phthalazin-1-one 666851-19-0P,
6-[4-[4-[3-(3,4-Dimethoxyphenyl)-6-0xo-5,6-dihydro-4H-pyridazin-1yl]piperidin-1-yl]1-4-oxobutoxyl-1H-quinolin-2-one 666851-37-2P,
(4AS, 8aR)-2-[1-[2-(2-Aminoethoxy)ethyl]piperidin-4-yl]-4-[3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one
RE: PAC (Pharmacological activity); SPN (Symthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)

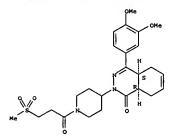
(Uses)
(prepn. of piperidine-substituted pyridazones and phthalazones as PDE4
inhibitors)
380227-17-8 CAPLUS
Piperidine, 1-[3-[(2-sminoethyl)thio]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

666850-88-0 CAPLUS
Piperidine, 4-[(465,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-{3-(methylsulfonyl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)



RN 666850-90-4 CAPLUS
CN 1(2H)-Phthalazinone,
2(1-[2-(2-benzofurany1)-2-oxoethy1]-4-piperidiny1]-4(3,4-dimethoxypheny1)-4a,5,8,8a-tetrahydro-, (4aS,8aR)- (9CI) (CA INDEX NAME)

666850-93-7 CAPLUS
1(2H)-Phthalazinome, 2-{1-{{4-(1H-benzimidazol-1-y1)phenyl}methyl}-4piperidinyl]-4-(1,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-,
monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) .

• HC1

666850-96-0 CAPLUS
2H-1,4-Benzoxazin-3(4H)-one, 6-[[4-[[4as,8aR]-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

666850-99-3 CAPLUS
4-Morpholinecarboxamide, N-[2-[[3-[4-[(485,8aR)-4-(3,4-dimethoxyphenyl)-4,5,8,8a-tetrahydro-1-oxo-2(IR)-phthalazinyl]-1-piperidinyl]-3-oxopropyl]sulfonyl]ethyl]- (9CI) (CA INDEX NAME)

RN 666851-03-2 CAPLUS
CN Piperidine,
1-[[(1,2-dihydro-2-oxo-6-quinolinyl)oxy]acetyl]-4-[(4aS,8aR)-4(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(lH)-phthalazinyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

666851-05-4 CAPLUS
Piperidine, 1-[4-[(1,2-dihydro-2-oxo-6-quinolinyl)oxy]-1-oxobutyl]-4[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)phthalazinyl]- (9CI) (CA INDEX NAME)

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN INDEX NAME) (Continued)

Absolute stereochemistry

• HCl

RN 666851-12-3 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2(methylthio|ethyl]-4-piperidinyl}-, monohydrochloride, (4aS,8aR)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

• HCl

RN 666851-15-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[2-

Habte

L4 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

666851-07-6 CAPLUS
1(2H)-Phthalazinone, 2-[1-[2-(2-aminoethoxy)ethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, dihydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

●2 HC1

RN 666851-10-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(2-methoxyethyl)-4-piperidinyl]-, monohydrochloride, (4as,8aR)- (9CI) (CA

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) (methylaulfonyl)ethyl)-(-piperidinyl)-, monohydrochloride, (4aS,8aR)-(9CT) (CA INDEX NAME)

Absolute stereochemistry.

RN 666851-17-8 CAPLUS
CN 1(2H)-Phthalazinone,
-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrehydro-2-[1-[2(2-hydroxyethoxy)ethyl]-4-piperidinyl]-, (4eS,8eR)- (9CI) (CA INDEX

Absolute stereochemistry.

666851-19-0 CAPLUS
Piperidine, 1-[4-[(1,2-dihydro-2-oxo-6-quinolinyl)oxy]-1-oxobutyl]-4-[3-(3,4-dinethoxyphenyl)-5,6-dihydro-6-oxo-1(4H)-pyridazinyl]- (9CI) (CA INDEX NAME)

02/09/2007

666851-37-2 CAPLUS
1(2H)-Phthalazinone, 2-[1-[2-(2-aminoethoxy)ethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

380226-97-1P, (4AS,8aR)-4-(3,4-Dimethoxyphenyl)-2-{piperidin-4-yl}4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride
380227-13-4P, (4AS,8aR)-4-(3,4-Diethoxyphenyl)-2-piperidin-4-yl4a,5,8,8a-tetrahydro-2H-phthalazin-1-one hydrochloride
666735-60-0P 666750-56-7P, 6-(3,4-Dimethoxyphenyl)-5methyl-2-{piperidin-4-yl}-4,5-dihydro-2H-pyridazin-3-one hydrochloride
666750-57-6P, 6-(3,4-Dimethoxyphenyl)-2-{piperidin-4-yl}-4,5dihydro-2H-pyridazin-3-one hydrochloride 666750-59-P,
6-(7-Methoxy-2,2-dimethyl-2,3-dihydrobenzofuran-4-yl)-2-{piperidin-4-yl}-4,5-dihydro-2H-pyridazin-3-one hydrochloride
RL: RCT (Reactant) SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
[preparation of piperidine-substituted pyridazones and phthalazones

DE4 inhibitors) 380236-97-1 CAPLUS 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-

L4 ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Con CN 1(2H)-Phthalazinone, (Con 1(2H)-Phthalazinone, (Con 4(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aR,8aS)-rel-{9CI} (CA INDEX NAME) (Continued)

Relative stereochemistry.

● HCl

666750-56-7 CAPLUS 3(2H)-Pyridazinome, 6-(3,4-dimethoxyphenyl)-4,5-dihydro-5-methyl-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

• HC1

RN 666750-57-8 CAPLUS
CN 3(2H)-Pyridazinone,
6-(3,4-dimethoxyphenyl)-4,5-dihydro-2-(4-piperidinyl), monohydrochloride (9CI) (CA INDEX NAME)

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) piperidinyl)-, monohydrochloride, (4aS,8aR)-.(9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HCl

380227-13-4 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HCl

666735-60-0 CAPLUS

ANSWER 14 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

• HC1

666750-58-9 CAPLUS
3(2H)-Pyridazinone,
3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)4,5-dihydro-2-(4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

HC1

REFERENCE COUNT: THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE PORMAT

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:719308 CAPLUS
DOCUMENT NUMBER: 139:240373
Pharmaceutical composition of a phosphodiesterase 4
historiae (PDE4) inhibitor or a PDE3/4 inhibitor and a

receptor antagonist for the treatment of respiratory diseases
Beume, Rolf; Bundschuh, Daniela; Weimar, Christian; Wollin, Stefan-lutz
Altana Pharma Ag, Germany
PCT Int. Appl., 87 pp.
CODEN: PIXXD2
Patent

INVENTOR (S):

PATENT ASSIGNEE(S): SOURCE:

Patent English

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PAI	ENI.	NPOR	M111	OIN:														
												LICAT						
												2003-						
												, DZ,						
												, NZ,						
				YU.														
		RW:	AM,	AZ,	BY,	KG,	KZ,	MD,	RU,	TJ,	TM	, AT,	BE,	BG,	CH,	CY,	cz,	DE,
			DK,	EE,	ES,	FI,	PR.	GB,	GR,	HU,	ΙE	. IT.	LU,	MC,	NL,	PT,	SE,	SI,
			SK,	TR														
												2003 -						
	AU	2003	2122	68		A1		2003	0916		AU :	2003 -	2122	68		2	0030	225
	EP											2003 -						
		R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR	, IT,	LI,	LU,	NL,	SE,	MC,	PT,
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		2004				A		2004	1206			2004 -						
PRI	ORIT	Y APP	LN.	INPO	. :						EP.	2002-	4987			A 2	0020	306

WO 2003-EP1876

W 20030225

The invention discloses the combined administration of PDE4 or PDE3/4 inhibitors and histamine receptor antagonists for the treatment of respiratory diseases.
449760-14-9 449760-15-0 449760-16-1
449760-17-2 449760-19-4 449760-20-7
449760-22-9 449760-23-0 449760-24-1
449760-25-2 449760-23-0 449760-24-1
449760-29-6 449760-10-9 449760-35-4
449760-40-1 449760-40-149760-35-4
449760-40-1 449760-40-49760-50-3
449760-51-4 449760-52-5 449760-50-3
449760-51-4 596102-05-9 449760-50-3
649760-51-4 596102-07-7 596102-09-9
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyll- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-17-2 CAPLUS 1-Piperidinepentanoic acid, (485,881,94-(3,4-diethoxyphenyl)-48,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-5-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Absolute stereochemistry.

RN 449760-15-0 CAPLUS
CN Piperidine,
4-[(4aS,8aP,4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-[(4a8,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-20-7 CAPLUS
1-Piperidinecarboxamide, 4-{(4as,BaR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N-phenyl-(9CI) (CA INDEX NAME)

449760-22-9 CAPLUS .
1-Piperidinecarboxamide, 4-{(4eR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

449760-23-0 CAPLUS
Piperidine, 4-[(4aS,8aR]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1cxo-2(1H)-phthalazinyl]-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl](SCI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

RN 449760-26-3 CAPLUS
CN Morpholine,
4-{[4-{(4aS,8aR)-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro1-0x0-2(1H)-phthalazinyl}-1-piperidinyl]carbonyl}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

RN 449760-24-1 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-28-5 CAPLUS
1(2H)-Phthelazinone,
4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(1-methyl-1H-pyrazolo{3,4-d}pyrimidin-4-yl)-4-piperidinyl}- (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 2-A

449760-29-6 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5.8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 2-A

RN 449760-30-9 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-(2-

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN NAME) (Continued)

Absolute stereochemistry.

449760-42-3 CAPLUS 2,3-Piperazinedione, 1-[[4-[(4aS,8aR]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-0x0-2[lff]-phthalazinyl]-1-piperidinyl]carbonyl]-4-ethyl-(9Cl) (CA INDEX NAME)

RN 449760-47-8 CAPLUS
CN Piperidine,
4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl]-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) pyrimidinyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[[4-[[48,5aR]-4-(3,4-diethoxyphenyl]-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-40-1 CAPLUS
1-Piperidineactamide, 4-[(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N-(1-methylethyl)- (9CI) (CA INDEX

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS OR STN (Continued)

449760-48-9 CAPLUS 1(2H)-Phthalazinone, 2-[1-[2-(4-amino-3,5-dichlorophenyl]-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(SCI) (CA INDEX NAME)

RN 449760-49-0 CAPLUS
CN 1(2H)-Phthalazinone,
4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-2-{1-{(2000-2H-1-benzopyran-7-yl)methyl}-4-piperidinyl}-, (4aS,8aR)- (9CI) (CA
INDEX NAME)

449760-50-3 CAPLUS

CN Morpholine,
4-[[4-[[4-5,8aR]-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro1-oxo-2(lH)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3, 4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-56-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4[1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-[[[4-{[4as,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethylester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-52-5 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3pyridinylmethyl)-4-piperidinyl]-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalezinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-58-1 CAPLUS
1-Piperidineactamide, 4-[(4eS,8aR)-4-(1,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

596102-01-1 CAPLUS
1(2H)-Phthalarinone,
,4-dimethackyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{1-methylethyl}-4-piperidinyl]- (9CI) (CA INDEX NAME)

Habte

596102-07-7 CAPLUS

OF Piperidine, 4-[(48, 68R)-4-(3, 4-diethoxyphenyl)-48,5,8,8a-tetrahydro-1-oxo-21(H)-phthalazinyl]-1-(4-morpholinylacetyl)- (9C1) (CA INDEX NAME)

Absolute stereochemistry.

RN 596102-09-9 CAPLUS
CN Piperidine,
4-[(4as, 8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl]-1-[[4-[2-(dimethylamino)ethyl]-1-piperazinyl]acetyl](9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2002:832801 CAPLUS DOCUMENT NUMBER: 137:337906

eparation of phthalazinones as phosphodiesterase

INVENTOR (5):

inhibitors.
Ratzelmann, Armin; Marx, Degenhard; Steinhilber, Wolfram; Steek, Geert Jan
Altana Pharma A.-G., Germany
PCT Int. Appl., 42 pp.
CODEN: PIXXD2
Patent
English PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

DATE PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2002085906 A2 20021031 WO 2002-EP4438 20020423
WO 2002085906 A3 20021199
M: AE. AL, AU, BA, BG, BR, CA, CN, CO, CU, CZ, DZ, EC, EE, GE, HR,
HU, ID, IL, IN, IS, JP, KR, LT, LV, MA, MK, MX, NO, NZ, PH, PL,
RO, SG, SI, SK, TN, UA, US, VN, YU, ZA, ZM, AM, AZ, BY, KG, KZ,
MD, RU, TJ, TM
RN: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, TR
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ER 2002009149 A 20040902 JP 2002-503433 20020423
UZ 529221 A 20040902 JP 2002-503221 20020423
UZ 5204127707 A1 20040701 US 2003-4775657 20031024
ED 1002094 A 20040930 ND 2003-4773 20031024
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ED 1002094 A 20040909 DA 2003-6930 20031117
IN 2003NN01079 A 20050429 IN 2003-8930 20031117
IN 2003NN01079 A 20050429 IN 2002-EP4438 W 20020423 PATENT NO.

WO 2002-EP4438

OTHER SOURCE(S):

MARPAT 137:337906

ANSWER 15 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

REFERENCE COUNT:

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L4 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

AB Title compds. (I; R1 = alkoxy, fluoroalkoxy; R2 = F, Br, C1; R3, R4 = H; R3R4 = bond; R5 = alkyl, cycloalkyl, cycloalkylmethyl, alkenyl, alkynyl, phenylalkenyl, polycycloalkyl, naphthyl, pyridyl, pyrazinyl, pyridazinyl, pyriddinyl, etc.), were prepared Thus, cis-4-(3-chloro-4-methoxyphenyl)-2- piperidin-4-yl-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one (preparation given) was atirred 16 h with morpholine-4-carbonyl chloride in pyridine to give

-4-(3-chloro-4-methoxyphenyl)-2-[1-(1-morpholin-4-ylmethanoyl)piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one. The latter inhibited

and PDE7 with -log ICSO = 8.64 and 7.64, resp. 474122-96-8P 474122-97-9P 474122-98-0P 474122-99-1P 474123-17-6P 474123-26-7P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(Uses) (preparation of phthalazinones as phosphodiesterase 4/7 inhibitors) 474122-96-8 CAPUS (Morpholine, 4-[[4-[(4sR.8aS)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8s-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry

RN 474122-97-9 CAPLUS
CN Piperidine,
-[(4ax,8a5)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(IN)-phthalszinyl]-1-[(4-methylphenyl)sulfonyl]-, rel- (9CI) (CA

Relative stereochemistry.

W 20020423

474122-98-0 CAPLUS
Piperidine, 1-acetyl-4-[(4aR,8aS)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

474122-99-1 CAPLUS
(1(2H)-Phthalazinone, 4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-2[1-(4-pyridinylmethyl)-4-piperidinyl]-, (4aR,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

●x HCl

474123-18-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of phthalazinones as phosphodiesterase 4/7 inhibitors)
474123-18-7 CAPLUS
1(3H)-Phthalazinone, 4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, (4aR,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

ANSWER 16 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 474123-17-6 CAPLUS
CN Piperidine,
4-[(4aR,8aS)-4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-[(2-oxo-1-imidazolidinyl)carbonyl]-, rel(9CI) (CA INDEX NAME)

Relative stereochemistry

474123-26-7 CAPLUS
1(2H)-Phthalazinone, 4-(3-chloro-4-methoxyphenyl)-4a,5,8,8a-tetrshydro-2[1-(4-pyridinylmethyl)-4-piperidinyl]-, hydrochloride, (4aR,8aS)-rel(9CI) (CA INDEX NAME)

Relative stereochemistry.

L4 ANSWER 17 OP 22 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:637671 CAPLUS
DOCUMENT NUMBER: 137:185496
TITLE: Preparation of piperidinyl benzopyridazine
derivatives

as PDE4 inhibitors for treatment of airway disorders Hatzelmann, Armin; Bundschuh, Daniela; Kley, Hans-peter; Timmerman, Hendrik; Christiasna, Johannes A. M.; Grundler, Gerhard; Gutterer, Beate; Sterk, Geert Jan Byk Gulden Lomberg Chemische Fabrik Gmbh, Germany PCT Int. Appl., 41 pp. CODEN: PIXXD2
PAtent
English INVENTOR(S):

PATENT ASSIGNEE(S): SOURCE:

DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

																	DATE	
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	WO	2002	0645	84		A1		2002	0822		WO 2	2002-	EP15	47			20020	214
		W:	AE.	AL.	AU.	BA.	BG,	BR,	CA.	CN.	co.	CU.	CZ.	DZ.	EC.	EB	. GE.	HR.
			HU.	ID.	IL.	IN.	IS.	JP.	KR.	LT.	LV.	MA.	MK.	MX.	NO.	NZ	, PH,	PL.
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					TJ.								-					
		RW:	AT.	BE.	CH.	CY.	DE.	DK.	ES.	PI.	FR.	GB.	GR.	IE.	IT.	ш	, MC,	NL.
			PT.	SE.	TR													
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	BR	2002	0072	78		A	•	2004	0210		BR 2	3002-	7278				20020	214
	JP	2004	5187	27		T		2004	0624		JP 2	1002-	5645	15			20020	214
	CN	1524	080			Ā		2004	0825		CN 2	2002-	8050	38			20020	214
	NZ	5274	24			A		2005	0225		NZ 2	2002-	5274	24			20020	214
	IN	2003	MNOO	668		A		2005	0211		IN 2	2003 -	MN66	8			2003	701
	US	2004	0679	46		Al		2004	0408		us a	2003 -	4678	32			20030	813
	us	6953	853			R2		2005	1011									
	NO	2003	0036	18		Ā		2003	1015		NO 2	2003 -	3618				2003 2003	814
	BG	1081	24			A		2004	0831		BG 2	2003-	1081	24			2003	821
	ZA	2003	0068	15		A		2004	0617		ZA 2	2003-	6815				20030	901
	US	2005	2340	62		A1		2005	1020		us a	2005-	1437	21			2003( 2005( 2001(	603
RIO	RIT	APP	LN.	INPO							EP 2	2001-	1034	96		Α.	2001	215
																		-
											NO 2	2002-	EP15	47		H	2002	214
											U5 2	2003-	4678	54		n.i	2003	JB 13

MARPAT 137:185496

Piperidinyl benzopyridazine derivs. [I; wherein R1 and R2 = H, or

her form an addnl. bond; R3 = substituted benzene, benzopyran derivative; R4

(C1-C4)alkoxy, optionally substituted with fluorine) were prepared (C1-C4)almoy, Optamer, Thus, to a solution of (485,8aR)-4-(3,4-diethoxyphenyl)-2-piperidin-4-yl-4a.5,8,8a-tetrahydro-2H-phthalaxin-1-one hydrochloride (synthetic preparation given) and p-TsCl in pyridine is stirred to give (4a5,8aR)-4-(3,4-diethoxyphenyl)-2-

p-TsCl in pyridine is stirred to give (4aS,8aR)-4-(3,4-diethoxyphenyl)-2[1-{toluene-4-sulfonyl}-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin1-one. The prepared compds. are effective PDE4 inhibitors useful in the treatment of airway disorders.

IT 449760-14-9P 449760-15-0P 449760-16-1P
449760-17-2P 449760-12-9P 449760-22-9P
449760-20-0P 449760-21-9P 449760-22-9P
449760-23-0P 449760-27-4P 449760-28-5P
449760-23-0P 449760-31-0P
449760-32-P 449760-31-0P
449760-32-P 449760-31-0P
449760-32-P 449760-31-P
449760-35-4P 449760-33-2P 449760-34-3P
449760-35-4P 449760-33-9P 449760-41-2P
449760-36-1P
449760-41-2P 449760-35-9P 449760-43-P
449760-41-2P 449760-47-8P 449760-48-9P
449760-49-0P 449760-51-6P
449760-55-8P 449760-51-6P
449760-55-8P
449760-51-6P

(preparation of piperidinyl benzopyridazine derivs. as PDE4

(preparation of piperidiny) be inhibitors for treatment of airway disorders) RN 449760-14-9 CAPLUS

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

RN 449760-17-2 CAPLUS
CN 1-Piperidinepentanoic acid,
4-[(4a5,8aR]-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl]-8-oxo- [9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-18-3 CAPLUS
CN Piperidine,
4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-21H]-phthalazinyl]-1-(4-pyridinylcarbonyl)-, conohydrochloride (9CI)

INDEX NAME)

Absolute stereochemistry.

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
Piperidine,
465, 8aR) -4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalazinyl)-1-[(4-methylphenyl)sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-15-0 CAPLUS CN Piperidine, 4-[{4a5,8aR]-4-{3,4-diethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-16-1 CAPLUS
Piperidine, 1-acetyl-4-[(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-19-4 CAPLUS
1-Piperidinecarboxamide, 4-{(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-N-(1,1-dimethylethyl)- (9CI) (CA

Absolute stereochemistry.

449760-20-7 CAPLUS
1-Piperidinecarboxamide, 4-[{4as,8aR}-4-(3,4-diethoxyphenyl)-4a,5,8,8a-terrahydro-1-oxo-2(1H)-phthalazinyl]-N-phenyl- (SCI) (CA INDEX NAME)

449760-21-8 CAPLUS
1-Piperidinecarboxamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-terrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)- (9CI) (CA INDEX RAME)

Absolute stereochemistry.

449760-22-9 CAPLUS 1-Piperidinecarboxamide, 4-{(4aR,8aS)-4-(2,3-dihydro-7-methoxy-2,2-

dimethyl-4-benzofuranyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-N-(1,1-dimethylethyl)-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 2-A

RN 449760-24-1 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(4-nitrophenyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-25-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{4pyridinylmethyl)-4-piperidinyl}-, {4aS,8aR}- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-23-0 CAPLUS
Piperidine, 4-[(485,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-[[5-(dimethylamino)-1-naphthalenyl]sulfonyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

N 449760-26-3 CAPLUS N Morpholine, -[{4-{468,8gR}-4-(3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-0x0-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl}- (9CI) (CA INDEX NAME)

449760-27-4 CAPLUS 1(2H)-Phthalazinone, 2-(1-[2-(4-amino-3,5-dichlorophenyl)-2-oxoethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, monohydrochloride, (4a5,8aR)- (9CI) (CA INDEX NAME)

RN 449760-28-5 CAPLUS
CN 1(2H)-Phthalazinone,
4(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{1methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

PAGE 2-A

449760-29-6 CAPLUS

1(2R)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-thieno[2,3-d]pyrimidin-4-yl-4-piperidinyl)-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

PAGE 1-A

RN 449760-30-9 CAPLUS
CN 1(2H)-Phthalazinome.
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2-pyrimidinyl}--piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

(Continued) L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-31-0 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-{2oxo-2R-1-benzopyran-7-yl}methyl]-4-piperidinyl}-, monohydrochloride,
(4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

• HCl

RN 449760-32-1 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-(1-methyl)-4-piperidinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

● HC1

RN . 449760-33-2 CAPLUS
CN Morpholine,
4-[4-{(485,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]-, monohydrochloride (9CI)
(CA INDEX NAME)

Absolute stereochemistry.

RN 449760-34-3 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(2-phenylethyl)-4-piperidinyl]-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN INDEX NAME) (Continued)

Absolute stereochemistry.

●2 HCl

RN 449760-37-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2-pyridinylmethyl}-4-piperidinyl]-, dihydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-38-7 CAPLUS
CN Morpholine,
4-{[4-{(4aS,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-

Habte

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

• HC1

RN 449760-35-4 CAPLUS
CN Morpholine,
4-[[4-[485,88R)-4-(3,4-diethoxyphenyl]-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl]- (9Cl) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-36-5 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4e,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl)-, dihydrochloride, (4as,8aR)- (9CI) (CA

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) oxo-2(1H)-phthelazinyl)-1-piperidinyl)acetyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-39-8 CAPLUS
CN 1-Piperazineethanamine,
4-[(4-[(485,88R)-4-(3,4-diethoxyphenyl)-48,5,8,88tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-piperidinyl]acetyl]-N,N-dimethyl-,
trihydrochloride (9CI) (CA INDEX NAME)

ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued) PAGE 2-A

449760-40-1 CAPLUS
1-Piperidineacetamide, 4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-N-(1-methylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-41-2 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-[[4(1,2,3-thiadiazol-4-yl)phenyl]methyl]-4-piperidinyl]-, dihydrochloride,
(4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN Absolute stereochemistry. (Continued)

• HCl

449760-44-5 CAPLUS
1-Piperidineacetamide, 4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

● HCl

RN 449760-47-8 CAPLUS
CN Piperidine,
4-[(4a5,8aF)-4-(1,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo2(1H)-phthalarinyl}-1-(4-pyridinylcarbonyl)- (9CI) (CA INDEX NAME)

Habte

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-42-3 CAPLUS 2,3-Piperazinedione, 1-[{4-[{4aS,8aR}-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]carbonyl}-4-ethyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

449760-43-4 CAPLUS
Benzoic acid, 4-[[[4-[[4as,8aR]-4-[3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(IRI-phthalazinyl]-1-piperidinyl]acetyl]amino]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

449760-48-9 CAPLUS
1(2H)-Phthalazinone, 2-{1-{2-(4-amino-3,5-dichlorophenyl}-2-oxoethyl}-4-piperidinyl}-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-(9CI) (CA INDEX NAME)

RN 449760-49-0 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxypheny)-4a,5,8,8a-tetrahydro-2-[1-[(2-cxo-2H-1-benzopyran-7-y1)methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

02/09/2007

RN 449760-50-3 CAPLUS

N Morpholine,
4-[[4-([468,88R)-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-51-4 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(1-(2-phenylethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-52-5 CAPLUS . CN 1(2H)-Phthelazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-(3-pyridinylmethyl)-4-piperidinyl]-, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 449760-53-6 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-[1-{2pyridinylmethyl)-4-piperidinyl]-, (4a5,8aR)- (9CI) (CA INDEX NAME)

(Continued) ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

RN 449760-54-7 CAPLUS
CN Morpholine,
4-[[4-[(48,8aR)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-1oxo-2(1H)-phthalazinyl]-1-piperidinyl]acetyl]- (9CI) (CA\_INDEX\_NAME)

Absolute stereochemistry.

RN 449760-55-8 CAPLUS
CN 1-Piperazineethanamine,
4-[4-[48,8aR]-4-(3,4-diethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl)-1-piperidinyl]acetyl]-N,N-dimethyl(9C1) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-56-9 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-{1-[4-(1,2,3-thiadiazo1-4-y1)phenyl]methyl]-4-piperidinyl]-, (4aS,8aR)- (9CI)
(CA INDEX NAME) .

Absolute stereochemistry.

449760-57-0 CAPLUS
Benzoic acid, 4-{[{4-{[4a.8aR]-4-{3.4-dimethoxyphenyl}-4a.5.8.8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}-1-piperidinyl]acetyl]amino}-, ethylester (9CI) (CA INDEX NAME)

449760-58-1 CAPLUS
1-Piperidineactamide, 4-[(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

IT 380226-97-1P 380227-12-3P 380227-13-4P
449760-45-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinyl benzopyridazine derivs. as PDE4 inhibitors for
treatment of airway disorders)
RN 380226-97-1 CAPLUS
N1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 449760-45-6 CAPLUS
CN 1(2H)-Phthalazinone,
4(2,3-dihydro-7-methoxy-2,2-dimethyl-4-benzofuranyl)48,5,8,8a-tetrahydro-2-(4-piperidinyl)-, (4aR,8aS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L4 ANSWER 17 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

● HC1

380227-12-3 CAPLUS

RN 380227-12-3 CAPLUS CN Piperidine, 1-(chloroacety1)-4-[(4eS,8aR)-4-(3,4-diethoxypheny1)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalaziny1}- (9CI) (CA INDEX NAME)

380227-13-4 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSMER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN
ACCESSION NUMBER: 2001:904118 CAPLUS
DOCUMENT NUMBER: 136:37625
TITLE: Preparation of pyridazinones as

136:37625
Preparation of pyridazinones as β2-adrenoreceptor agonists and PDE4 inhibitors
Hatzelmann, Armin; Bundschuh, Daniela; Eltze,

INVENTOR(S): Manfrid;

Van der Laan, Yvonne; Timmermann, Hendrik; Christiaans, Johannes; Brundel, Paulus; Sterk, Geert Byk Gulden Lomberg Chemische Pabrik G.m.b.H., PATENT ASSIGNEE(S): Germany;

Byk Nederland B.V. PCT Int. Appl., 79 pp. CODEN: PIXXD2 Patent English SOURCE:

DOCUMENT TYPE: LANGUAGE:

LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

WO 2001094	319	A1	20011213	WO 2001-EP6230	20010601
W: AE	, AL, AU,	BA, BG	, BR, CA,	CN, CO, CU, CZ, EC.	EE, GE, HR, HU,
ID	, IL, IN,	IS, JP	KR. LT.	LV, MK, MX, NO, NZ,	PL. RO. SG. SI.
SK	, UA, US,	VN, YU	, ZA, ZW,	AM, AZ, BY, KG, KZ,	MD, RU, TJ, TM
CA 2411351		A1	20011213	CA 2001-2411351	20010601
BR 2001011	440	A	20030603	BR 2001-11440	20010601
JP 2003535	850	T	20031202	JP 2002-501869	20010601
HU 2003012	40	A2	20031229	HU 2003-1240	20010601
NZ 522882		A	20040730	NZ 2001-522882	20010601
IN 2002MNO	1591	A	20050318	IN 2002-MN1591	20021111
ZA 2002009	598 '	A	20030729	ZA 2002-9598	20021126
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				EP 2000-111795	A 20000605
				WO 2001-EP6230	W 20010601
OTHER SOURCE(S)		MARPAT	136:3762	5	
	WO 2001094 W: AE ID SK RW: AT PT CA 2411315 EP 1296956 R: AT IE BR 2001011 JP 2003515 HU 2003515 HU 2003512 IN 2522882 IN 2002009 NO 2002005 US 20031256 PRIORITY APPLN.	WO 2001094319 W: AR. AL, AU, ID, IL, IN, SK, UA, US, RW: AT, EE, CH, PT, SET CA 2411351 EP 1296956 R: AT, BE, CH, IE, SI, LT, BR 2001011440 JP 2003535850 HU 200201240 NY 522862 IN 2022009598 NO 2002005811 US 200319562 US 69313266 PRIORITY APPLN. INFO::	WO 2001094319 A1  W: AE, AL, AU, BA, BG  ID, IL, IN, IS, JP  SK, UA, US, VN, YU  RW: AT, BE, CH, CY, DE  PT, SE TF  CA 2411351 A1  EP 1296956 A1  R: AT, BE, CH, DE, DK  IE, SI, LT, LV, PI  BR 2001011440 A2  JP 2003535850 T  HU 200301240 A2  NZ 52282 A  IN 200200511 A  NO 200200511 A  US 6931296 B2  PRIORITY APPLN. INFO.:	WO 2001094319 A1 20011213 W: AR, AL, AU, BA, BG, BR, CA, ID, IL, IN, IS, JP, KR, LT, SK, UA, US, VN, YU, ZA, ZM, RM: AT, BE, CH, CY, DB, DK, ES, PT, SE IR  CA 2411355 A1 20011213 EP 1296956 A1 20031020 R: AT, BE, CH, DE, DK, ES, FR, IE, SI, LT, LY, PI, RO, MK, BR 2001011440 A 20030603 JP 2003513850 T 20031229 HU 200301240 A2 20031229 NZ 522862 A 20040730 IN 2020M051591 A 20050318 ZA 2002005811 A 200310204 US 2003195215 A1 200310204 US 2003195215 A1 20031026 US 6931296 B2 20050823 PRIORITY APPLN. INFO.:	CA 2411351 EP 1296956 A1 200310402 EP 2001-936419 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, IE, SI, LT, LV, PI, RO, MK, CY, AL, TR BR 2001011440 A 20030603 BR 2001-11440 AJP 2003535850 T 200311202 BR 2001-11440 AZ 20031229 BR 2003-11440 AZ 20031229 BR 2003-11440 AZ 20031229 BR 2002-951869 AZ 200309598 AZ 200309598 AZ 200309598 AZ 200309598 BR 2003195296 BR 200309598 BR 2003195296 BR 200309598 BR 2003195296 BR 200309598 BR 2003195296 BR 200309598 BR 200309598 BR 200319529 B

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The title compds. [I; Arl = substituted Ph, dihydrobenzofuranyl; R6, R7 = H, alkyl; or R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form II-V; A = ChHZmYXChH2n, YXCm52m2ChH2n; X = a bond, O, S, etc.; Y = a bond, phenylene, cycloalkylene, etc.; Z = 0, S, SO2, etc.; m = 0-4; n = 1-4; R8 = H, alkyl;

Ar2 = 8-hydroxy-IH-quinolin-2-on-5-yl, substituted Ph], useful as novel effective bronchial therapeutics, were prepared The general procedures

ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) prepn. of compds. I such as (cis)-VI.fumarate were described. Biol. data for compds. I were given.
380226-56-29 380226-64-29 380226-65-3P
380226-79-29 380226-69-79 380226-71-1P
380226-72-29 380226-74-4P 380226-77-7P
380226-78-8P 380226-30-2P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridszinones as β2-adrenoreceptor sqonists and PDE4

(Uses) (preparation of pyridazinones as β2-adrenoreceptor agonists and PDE4 inhibitors) 360246-56-2 CAPLUS Piperidine, 1-(4-[(2-(4-amino-3-chloro-5-cyanophenyl)-2-hydroxyethyl]amino|-1-coxobutyl]-4-((485,587)-4-(3,4-dimethoxyphenyl)-48,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-, (2E)-2-butenedioste

(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-55-1 CMF C34 H41 C1 N6 O5

Absolute stereochemistry.

CM 2

CRN 110-17-8 CMF C4 H4 O4

Double bond geometry as shown.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

hydroxyethyl]amino]propyl]-4-{{4as,8aR}-4-{3,4-dimethoxyphenyl}-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

380226-67-5 CAPLUS
Piperidine, 1-[[[2-(4-amino-3,5-dichlorophenyl)-2-hydroxyethyl]amino]acetyl]-4-[[485,8aR]-4-(3,4-diethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2[HP]-phthalazinyl]-, [2E]-2-butenedioate [1:1] [salt] (9CI) (CA INDEX NAME)

CRN 380226-66-4 CMP C33 H41 C12 N5 O5

Absolute stereochemistry.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

380226-64-2 CAPLUS
1(2H)-Phthalazinone, 2-[1-[2-[{2-[{2-(4-amino-3,5-dichlorophenyl)-2-hydroxyethyl]amino]ethyl]sulfonyl]ethyl]-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, (4aS,8aR)-, (2E)-2-butenedioate (1:1) (salt) [9CI) (CA INDEX NAME)

CRN 380226-63-1 CMF C33 H43 C12 N5 O6 S

CM 2

CRN 110-17-8 CMF C4 H4 O4

Double bond geometry as shown.

380226-65-3 CAPLUS
1-Piperidinecarbothioamide, N-[3-[[2-(4-amino-3,5-dichlorophenyl)-2-

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CH 2

Double bond geometry as shown.

180226-69-7 CAPLUS
Piperidine, 1-[[2-[2-(4-amino-3,5-dichlorophenyl)-2hydroxyethyl]amino| ethyl]sulfonyl]-4-[(485,88R)-4-(3,4-dimethoxyphenyl)4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, (2E)-2-butenedioate

(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-68-6 CMP C31 H39 C12 N5 O6 S

CM 2

CRN 110-17-8 CMF C4 H4 O4

Double bond geometry as shown.

380226-71-1 CAPLUS
Piperidine, 1-[(2S)-2-[[2-(3,4-diamino-5-chlorophenyl)-2hydroxyethyl]amino]-1-0xopropyl]-4-[(485,88R)-4-(3,4-dimethoxyphenyl)4e,5.8,8a-tetrahydro-1-0xo-2(1H)-phthalazinyl)-, (2E)-2-butenedioate

(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-70-0 CMF C32 H41 C1 N6 O5

Absolute stereochemistry.

ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

380226-74-4 CAPLUS
Piperidine, 1-[3-[[2-[(2-(4-amino-3,5-dichlorophenyl)-2-hydroxyethyl]amino]ethyl]thio]-1-oxopropyl]-4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-,monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 2-A

• HC1

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CM 2

Double bond geometry as shown.

380226-72-2 CAPLUS
Piperidine, 4-[485,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1R)-phthalazinyl]-1-[2-[2-hydroxy-2-[4-hydroxy-3-(hydroxymethyl)phenyl]ethyl]amino]ethyl]sulfonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)

380226-77-7 CAPLUS
Piperidine, 1-[3-{(2-[[2-(4-amino-3-chloro-5-cyanophenyl)-2-hydroxyethyl]amino]ethyl]sulfonyl]-1-oxopropyl]-4-[(465,88R)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(H)-phthalazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

380226-78-8 CAPLUS
Piperidine, 1-[(2S)-2-[[2-(4-amino-3-chloro-5-cyanophenyl)-2-hydroxyethyl]amino]-1-0xopropyl]-4-[(4aS, 8aR]-4-[3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-0xo-2(1H)-phthalazinyl]-, monohydrochloride (9CI)(CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

Habte

● HC1

RN 380226-80-2 CAPLUS
CN Benzonitrile, 2-amino-3-chloro-5-{2-[[6-[4-[(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl|hexyl|amino|-1-hydroxyethyl]-, (2E)-2-butenedioate (1:1)
(salt) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-79-9 CMF C36 H47 C1 N6 Q4

Absolute stereochemistry.

CH 2

CRN 110-17-8

Double bond geometry as shown.

IT 380226-94-8P 380226-95-9P 380226-96-0P 380226-97-1P 380227-08-7P 380227-10-1P

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)
CN Carbamic acid, [4-[4-[(485,88R]-4-{3,4-dimethoxyphenyl]-48,5,8,8atetrahydro-1-xox-2[1H]-phhalazinyl]-1-piperidinyl]-4-xxobutyl]-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 380226-96-0 CAPLUS CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4s,5,8,8a-tetrahydro-2-(4piperidinyl)-. (4ss.8sR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 380226-97-1 CAPLUS
CN 1(2H)-Phthalazinone, 4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4aS,8aR)- (SCI) (CA INDEX NAME)

Absolute stereochemistry.

Habte

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) 380227-11-2P 380227-12-3P 380227-13-4P 380227-11-5P 380227-15-6P 380227-16-7P 380227-17-8P 380227-15-9P 380227-17-8P 380227-13-19-0P 180227-20-3P 380227-21-4P 9P 380227-21-4P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of pyridazinones as β2-adrenoreceptor agonists and PDE4 inhibitors)
RN 380226-94-8 CAPLUS
CN Piperidine, 1-(4-amino-1-oxobuty1)-4-[(4as,8ar)-4-(3,4-dimethoxypheny1)-4a,5,8,8a-tetrahydro-1-oxob-2(1H)-phthalaziny1)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 380226-93-7
CMF C25 H34 N4 O4

Absolute stereochemistry.

~

CRN 76-05-1

RN 380226-95-9 CAPLUS

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued

• HC1

RN 380227-08-7 CAPLUS
CN 1(2H)-Phthalazinone,
4-(3,4-dimethoxyphenyl)-2-[1-[2-(ethylsulfonyl)ethyl]4-piperidinyl]-4a,5,8,8a-tetrahydro-, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

N 380227-10-1 CAPLUS
N 1-Piperidinecarbothioamide, N-(4-aminobutyl)-4-[(4aS,8aR)-4-[3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CPI :

CRN 380227-09-8 CMF C26 H37 N5 03 S

02/09/2007

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) Absolute stereochemistry.

380227-11-2 CAPLUS Carbamic acid, [4-[[[4-[(4aS,BaR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]thioxomethyl]amino]buty l]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

380227-14-5 CAPLUS
Piperidine, 4-(1(485,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl)-1-(ethenylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

380227-15-6 CAPLUS
Piperidine, 1-[(2S)-2-amino-1-oxopropyl]-4-[(4aS,8aR)-4-{3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]- (9CI).
(CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

RN 380227-12-3 CAPLUS '
CN Piperidine,
1-(chloroacetyl)-4-[(485,88R)-4-(3,4-diethoxyphenyl)-48,5,8,8atetrahydro-1-oxo-2(1H)-phthalazinyl]- (SCI) (CA INDEX NAME)

Absolute stereochemistry.

380227-13-4 CAPLUS
1(2H)-Phthalazinone, 4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2-(4-piperidinyl)-, monohydrochloride, (4a5,8aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

380227-16-7 CAPLUS
Piperidine, 4-{(4aS,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-

oxo-2(1H)-phthalazinyl}-1-[(2S)-2-[[(1,1-dimethylethyl)amino]carbonyl]ami
no]-1-oxopropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

380227-17-8 CAPLUS
Piperidine, 1-[3-{(2-aminoethyl)thio}-1-oxopropyl}-4-{(4a5,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl}- (9CI) (CA INDEX NAME)

380227-18-9 CAPLUS
Carbamic acid, [2-[[3-[4-[[4as,8aR]-4-(3,4-dimethoxyphenyl]-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]-3oxopropyl]thio]ethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

RN 38027-19-0 CAPLUS
CN Piperidine,
1-[3-[(2-aminoethyl)sulfonyl]-1-oxopropyl]-4-[(4a5,8aR)-4-(3,4- dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-,
monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

● HC1

380227-21-4 CAPLUS
1H-180indole-1, 3(2H)-dione, 2-[6-[4-[(4as,8aR)-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-1-oxo-2(1H)-phthalazinyl]-1-piperidinyl]hexyl)-

(CA INDEX NAME)

Absolute stereochemistry.

REFERENCE COUNT:

THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

L4 ANSWER 18 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN

(Continued)

PAGE 1-A

PAGE 2-A

● HC1

380227-20-3 CAPLUS
1(2H)-Phthalazinone, 2-(1-(6-aminohexyl)-4-piperidinyl]-4-(3,4-dimethoxyphenyl)-4a,5,8,8a-tetrahydro-, monohydrochloride, (4as,8aR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSMER 19 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN ACCESSION NUMBER: 2001:483306 CAPLUS DOCUMENT NUMBER: 134:266260 Studies on isocyanides and relational facile Studies on isocyanides and related compounds; a

synthesis of 4-phenyl-1-(2H)phthalazinone-2-alkanoic acid amides Marcaccini, Stefano; Pepino, Roberto; Polo, Cecilia; Pozo, Ma Cruz CNR, Centro di Studio sulla Chimica e la Struttura AUTHOR(S):

CORPORATE SOURCE:

CORPORATE SOURCE:

COMPOSTI Eterociclici e loro Applicazioni,
Dipartimento di Chimica Organica "Ugo Schiff",
Universita di Pirenze, Plorence, 50121, Italy
SOURCE: Synthesis (2001), (1), 85-88
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCURENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:266260
AB A convenient synthesis of 4-phenyl-1-oxo-(2H)phthelazine-2-alkanoic amides
by the Ugi 4-component condensation (Ugi 4-CC) is reported. The reaction between acetaldehyde azine, 2-benzoylbenzoic acid, and cyclohexyl isocypanide spontaneously afforded N-cyclohexyl-2-(1,2-dihydro-1-oxo-4-phenylphthalazin-2-yl)propionamide upon elimination of McCho from the intermediate Ugi 4-CC adduct. Starting from less reactive azines arising from ketones, the corresponding Ugi 4-CC adducts did not spontaneously cyclize, whereas phenylacetaldehyde azine afforded a mixture of the Ugi 4-CC

adduct and cyclized product. In all of the cases, the adducts were

IT

ly cyclized in acidic medium.
332049-47-5P
RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of oxophthalazinealkanoic amides)
332049-47-5 CAPLUS

332049-47-5 CAPLUS
4-Piperidinecarboxamide, 1-acetyl-N-cyclohexyl-4-(1-oxo-4-phenyl-2(1H)-phthalazinyl)- (9CI) (CA INDEX NAME)

REFERENCE COUNT:

THERE ARE 28 CITED REFERENCES AVAILABLE FOR 28

RECORD. ALL CITATIONS AVAILABLE IN THE RE

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FORMAT

L4 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN OTHER SOURCE(S): MARPAT 129:136174 (Continued)

AB Title compds. [1; R1 = alkoxy, fluoroalkoxy; R2 = alkoxy, cycloalkylnethoxy, fluoroalkoxy; R3, R4 = H, or R3R4 = bond; R5 = R6, (CH2)aR7, (CH2)nCOR8, CH(R9)2, (CH2)pAr; R6 = H, alkyl, cycloalkyl, cycloalkylathyl, alkoyl), asphtyl, phenylalkenyl, pyridyl, pyrazinyl, indanyl, etc.; R7 = OH, halo, cyano, NO2, ONO2, CO2H, Pho, alkoxy, cycloalkoxy, alkylcarbonylamino, etc.; R8 = (substituted) Ph, naphthyl, phenanthryl, anthracenyl; R9 = (CH2)qPh; Ar = naphthyl, pyrazinyl, pyridazinyl, pyrimidinyl, quinazolinyl, cinnolinyl, isoquinolinyl, imidazolyl, pyrazolyl, oxazolyl, thiazolyl, furyl, thienyl, pyrrolyl, (substituted) Ph, etc.; m = 1-8; n = 1-4; p = 1-6; q = 0-2), were prepared Thus, cis-4-(3,4-dimethoxyphenyl)-2-propyl-4a,5,6,7,8,8a-hexahydro-2H-phthalazin-1-one (preparation outlined) inhibited PDE 4 with -log IC50 >7.5.

17 210466-87-8P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIO( [Riological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIO( [Riological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of srylphthalazinones as inhibitors of cyclic nucleotide phosphodiesterase)
RN 210466-87-8 CAPLUS
CN 1(2H)-Phthalazinone.
4-(3,4-dimethoxyphenyl)-4a,5,6,7,8,8a-hexahydro-2-(1-methyl-4-piperidinyl)-, (4aR,8aS)-rel-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CH 1

CRN 210466-86-7 CMF C22 H31 N3 03

Relative stereochemistry.

L4 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN
1998:509189 CAPLUS
129:136174
TITLE: 12916174
Preparation of arylphthalaxinones as inhibitors of cyclic nucleotide phosphodiesterase.
INVENTOR(S): 4 Van Der Mey, Margaretha; Van Der Lean, Ivonne
Johanne: 4 Van Der Mey, Margaretha; Van Der Lean, Ivonne

INVENTOR(S): Johanna;

Timmerman, Hendrik, Hatzelmann, Armin, Boss, Hildegard; Hafner, Dietrich; Beume, Rolf; Kley, Hans-Peter; Sterk, Geert Jan Byk Gulden Lomberg Chemische Fabrik G.m.b.H., Germany PCT Int. Appl., 59 pp. CODEN: PIXXD2 Patent English 1

PATENT ASSIGNEE (S): SOURCE:

DOCUMENT TYPE: LANGUAGE: PAMILY ACC. NUM. COU

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L4 ANSWER 20 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

CM 2

Double bond geometry as shown

REFERENCE COUNT:

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

WO 1998-EP124

W 19980112

L4 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2007 ACS ON STN
ACCESSION NUMBER: 1961:76261 CAPLUS
DOCUMENT NUMBER: 55:76261
ORIGINAL REFERENCE NO.: 55:1449la-e
Pyridazine derivatives
Sandoz Ltd.
PATENT ASSIGNEE(S): 584062 Ltd.
PATENT LANGUAGE: Unavailable
FAMILY ACC. NUM. COUNT: 1976084710N: DOCUMENT TYPE: LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE GB 858792 19610118 GB 1959-3664 19599202
Pyridazine derivs. showing slight toxicity and good analgetic action were prepared 1-Methyl-4-piperidylhydrazine (1) (55.6 g.) and 50 g. AcCH2CMMeCO2H refluxed 19 hrs. in alc., the alc. removed, the residue dissolved in CNC13, extracted with 2N HC1, made alkaline, extracted with CHC13, and

CRC13, and concentrated gave
4.6-dimethyl-2-(1-methyl-4-piperidyl)-4.5-dihydro-3(2H)pyridazinone, m. 107-11\*. This compound (10 g.) in 100 cc. AcOH
treated dropwise with 7.66 g. Br, the solvent removed at 100°, the
residue extracted from alkaline solution with CRC13, and chromatographed

residue extracted from alkaline solution with CHCl3, and chromatographed on Al203
gave 4,6-dimethyl-2-(1-methyl-4-piperidyl)-3(2H)-pyridazinone, m. 87-9°, HBr salt m. 250-2°. Similarly, I and the appropriate γ-oxobutyric acids gave the following 2-(1-methyl-4-piperidyl)-3(2H)-pyridazinones (substituents, m.p., and m.p. of 4,5-dihydro analog given): 6-Ph, 122-5° (HBr salt m. 310°), 153-5°, 4,6-Ph2, 122-3°, 138-60°, 4,6-Me2, (HCl salt m. 252-4°), 92-4° (HCl salt m. 246-50°); 4,6-MePh, 284°, 124°, 6-(p-MeoChH4), - (tartrate m. 199-200°), 107-8°; 6-(bromo-β-thienyl), - (HCl salt m. 286°), 103-5° (for 6-(β-thienyl) derivative); 4,5,6-Et2Ph, - (HCl salt m. 269-70°; HBr salt m. 262-4°), -; 4,6-PhMe, 140° (HCl salt m. 288°), 183-5°. I (55.73 g.) in 200 cc. alc. added dropwise at 15° to 37.15 g. Ac20 (II) in 200 cc. C6H6, the mixture kept overnight, and refluxed 15 min., the solvent removed, and the residue distilled in vacuo gave 2,3-butanedione mono(1-methyl-4-piperidylhydrazone)
mono(1-methyl-4-piperidylhydrazone)
(III), b0.2 125-30°. NCCH2CO2Et (11.3 g.), 16.4 g. III, 8.0 g. AcOH, and 5.13 g. NH4OAc refluxed 17 hrs. in 100 cc. C6H6 with separation of H20, concentrated at 50° in vacuo, the oil diluted with CHCl3, shaken

H2O, concentrated at 50° in vacuo, the oil diluted with CHCl3, shaken

with

2N NaOH, concentrated, and chromatographed on Al203 gave
4-cyano-5,6-dimethyl-2(1-methyl-4-piperidyl)-3(2H)-pyridazinone, m. 103-5° (Et20); HCl
salt m. 263-6°, HBr salt m. 238-5°. Similarly;
1,2-cyclohexanedione and I gave 1,2-cyclohexanedione mono(1-methyl-4piperidylhydrazone), b0.0° 112-20°, and 4-cyano-5,6cyclotetramethylene-2-(1-methyl-4-piperidyl)-3(2H)-pyridazinone (HCl salt
m. 247-50°). 1-Isopropyl-4-piperidylhydrazine and II gave
2,3-butanedione mono(1-isopropyl-4-piperidylhydrazone), m. 84-7°,

ANSWER 21 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued)

860411-95-6 CAPLUS 4-Pyridazinecarbonitrile, 2,3,4,5-tetrahydro-2-(1-methyl-4-piperidyl)-3-oxo-6-phenyl- (6C1) (CA INDEX NAME)

ANSWER 21 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) and 4-cyano-5,6-dimethyl-2-(1-isopropyl-4-piperidyl)-3(2H)-pyridazinone (hydrochloride m. 276-8°).
101268-89-7P, 3(2H)-Pyridazinone, 4,5-dihydro-2-(1-methyl-4-piperidyl)-6-phenyl-101599-83-1P, 3(2H)-Pyridazinone, 4,5-dihydro-4-methyl-2-(1-methyl-4-piperidyl)-6-phenyl-101599-90-0P, 3(2H)-Pyridazinone, 4,5-dihydro-6-(p-methoxyphenyl)-2-(1-methyl-4-piperidyl)-102556-73-9P, 3(2H)-Pyridazinone, 4,5-dihydro-2-(1-methyl-4-piperidyl)-4-(6-diphenyl)-860411-95-6P, 4-Pyridazinecarbonitrile, 2,3,4,5-tetrahydro-2-(1-methyl-4-piperidyl)-3-oxo-6-phenyloxo-6-phenyl-RL: PREP (Preparation) (preparation of)
101268-89-7 CAPLUS
3(2H)-Pyridazinone; 4,5-dihydro-2-(1-methyl-4-piperidyl)-6-phenyl- (6CI)
(CA INDEX NAME)

RN 101599-83-1 CAPLUS
CN 3(2H)-Pyridazinone,
4,5-dihydro-4-methyl-2-(1-methyl-4-piperidyl)-6-phenyl(6CI) (CA INDEX NAME)

0-0 CAPLUS 101599-90-0 dazinone, 4,5-dihydro-6-(p-methoxyphenyl)-2-(1-methyl-4-- (GCI) (CA INDEX NAME)

102556-72-9 CAPLUS
3(2H)-Pyridazinone, 4.5-dihydro-2-(1-methyl-4-piperidyl)-4.6-diphenyl-(6CI) (CA INDEX NAME)

ANSWER 22 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN SSION NUMBER: 1960:118213 CAPLUS MENT NUMBER: 54:118213 IRAL REFERENCE NO.: 54:22593b-1

ACCESSION NUMBER: DOCUMENT NUMBER: ORIGINAL REFERENCE NO.: TITLE:

OCCUMENT AUMBER: 94:11225)3-1

ORIGINAL REPERENCE No.: 54:22593b-1

TITLE: Synthetic drugs. V. Preparation of basically substituted 6-pyridazinones

AUTHOR(S): Jucker, E.; Suess, R.

CORPORATE SOURCE: Sandoz, Basel, Switz.

SOURCE: Helvetice Chimica Acta (1959), 42, 2506-14

CODEN: HCACAV: ISSN: 0018-019X

JOURNAL JO

of the prepared compds. showed analgesic properties. To a cooled solution of KCN in water β-benzoylacrylic acid was added with stirring. The precipitated K salt was filtered off, dissolved in water and treated with 2N HCl to give 62% α-cyano-β-benzoylpropionic acid, separated as an oil, m. 101-3° (Et20). trans-2-Benzoylcyclohexane-1-carboxylic acid (I) was prepared in 92% yield, m. 151-2° (Et20) as described by F. and N. (loc. cit.) for the cis epimer (II). I also was obtained from II by heating a solution in 2N NaOH for 16 hrs. at 100°. II was refluxed with N-methyl-4-piperidylhydranie in EtOH for 24 hrs. to precipitate 74% cis-1-(1-methyl-4-piperidyl)-3-pinenyl-4,5-tetramethylen-4,5-dihydro-6-pyridazinone (III). m. 146° (EtOH); the trans epimer (IV) was prepared in an analogous way in 78% yield, m. 155° (EtOH). To a solution of IV in AcOH a solution of Br in AcOH was added dropwise. The mixture

mixture

was heated 2 hrs. to 120°, AcOH removed by distillation and the residue recrystd. from H2O and EtOH to give 62½

1-(1-methyl-4-piperidyl)-3-phenyl4,5-tetramethyl-ene-6-pyridazinone-HBr (V), m. 220-2°; the free base m. 179-80° (acetone). V was obtained from III in 69½ yield. The following 1-(1-methyl-4piperidyl)-6-pyridazinone derivs. were prepared in this way: 3-methyl, m. 87-9° (after sublimation at 80° in high vacuo; 3-phenyl, m. 122-5° (acetone) (HBF salt decomposing 310° (H2O)]; 3,5-dimethyl (HCl salt, m. 252-4° (EtOH);
3-methyl-5-phenyl, m. 140° (Et20-petr. ether); 3-phenyl-5-methyl (HCl salt hydrate), m. 284° (EtOH); 3-phenyl-5-cyano, m. 223° (EtOH) (HCl salt decomposing 280° (H2O)); 3,5-diphenyl, m. 243° (acetone); 3-phenyl-4,5-diethyl (HCl salt hemihydrate), m. 268-70° (EtOH)]. The monohydrazone from biacetyl and N-methyl-4-piperidylhydratine. Et cyanoacetate, AcOH, and NH4OAc were refluxed 15 hrs. in benzene while water was removed continuously. The benzene was distilled and the residue taken up in CHCl3. The solution was

cooled and shaken with 20% KOH, 18% HCl, and 2N HCl, resp., made alkaline with 18% KOH and again extracted with CHCl3. After removing the CHCl3, the

was taken up in Et20, petr. ether added, and the solution filtered through an Al203-column. The filtrate was treated with a 30% HBr-AcOH solution to

46.0 g. 1-(1-methyl-4-piperidyl)-3,4-dimethyl-5-cyano-6-pyridazinone-HBr

L4 ANSWER 22 OF 22 CAPLUS COPYRIGHT 2007 ACS on STN (Continued) from 65.6 g. of the monohydrazone, decompg. 238-40\* (MeOH-Et2O); free base m. 103-5\* (Et2O). The following compds. were prepd. in this way: 1-(1-methyl-4-piperidyl)-3,4-tetramethylene-5-cyano-6-pyridazinone-HCl, decompg. 276-6\* (EtOH-Et2O); 1-(1-isopropyl-4-piperidyl)3,4-dimethyl-5-cyano-6-pyridazinone-HCl, decompg. 276-6\* (EtOH-Et2O), and 1-(1-methyl-2) dimethylaminoethyl)3,4-dimethyl-5-cyano-6-pyridazinone-HBr, m. 209-11\* (EtON).

17 879006-23-2P, 1(2N)-Phthalazinone, 4a,5,6,7,8,8a-hexahydro-2-(1-methyl-4-piperidyl)-4-phenyl-, trans-879006-25-4P, 1(2N)-Phthalazinone, 4a,5,6,7,8,8a-hexahydro-2-(1-methyl-4-piperidyl)-4-phenyl-, cis-RL: PREP (Preparation of)

RN 879006-23-2 CAPLUS

CN 1(2N)-Phthalazinone, 4a,5,6,7,8,8a-hexahydro-2-(1-methyl-4-piperidyl)-4-phenyl-, trans-(6CI) (CA INDEX NAME)

879006-25-4 CAPLUS 1(2H)-Phthalazinone, 4a,5,6,7,8,8a-hexahydro-2-(1-methyl-4-piperidyl)-4-phenyl-, cis- (6CI) (CA INDEX NAME)

Relative stereochemistry.